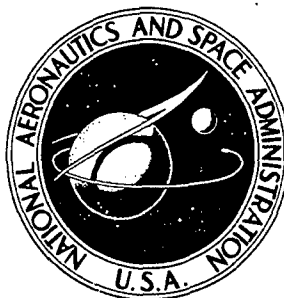


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**CLINICAL SPACE MEDICINE**

**A PROSPECTIVE LOOK AT MEDICAL PROBLEMS  
FROM HAZARDS OF SPACE OPERATIONS**

*by Douglas E. Busby*

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*Prepared by*

**LOVELACE FOUNDATION FOR MEDICAL EDUCATION AND RESEARCH  
Albuquerque, N. Mex.**

*for*

**NATIONAL AERONAUTICS AND SPACE ADMINISTRATION • WASHINGTON, D. C. • JULY 1967**

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By Douglas E. Busby, M. D., M. Sc.

Distribution of this report is provided in the interest of information exchange. Responsibility for the contents resides in the author or organization that prepared it,

Prepared under Contract No. NASr-115 by  
Department of Aerospace Medicine and Bioastronautics  
LOVELACE FOUNDATION FOR MEDICAL EDUCATION AND RESEARCH  
Albuquerque, N. Mex.

for

**NATIONAL AERONAUTICS AND SPACE ADMINISTRATION**

"In truth, we advance far by the harmonious  
assembling of facts made known by many  
observers and writers. "

Charles H. Mayo, 1918

## PREFACE

Many real and potential hazards will face astronauts\* during operations in space. Some of these hazards might be of little medical significance; others might produce serious medical problems.

In this report, an attempt is made to describe the characteristics and suggest the management in space of possible medical problems which might arise from hazards of space operations; attention will therefore not be given to possible naturally-occurring diseases. Writing is oriented to missions during which, due to the time required to return to Earth, the diagnosis and interim treatment of medical problems will have to be carried out in space. Therefore it is assumed in this report that diagnostic and treatment facilities will be available, and that advanced spacecraft concerned will provide a "shirtsleeve" environment in which multidisciplined crews, including medically-trained personnel, will be able to live in reasonable comfort.

To lay the groundwork of Clinical Space Medicine, a field in which very little has been written and no experience gained to date, this report covers more than just the clinical manifestations, diagnosis, and treatment of possible medical problems in space. Wherever necessary, various hazards of space operations are defined and analysed in order to determine their possible medical effects. The pathophysiologic characteristics of medical problems are discussed, frequently in detail, to provide the rationale for the prevention and treatment of the problems in space. Many pertinent basic medical facts are stated not only to refresh memories of physicians not actively engaged in the practice of medicine, but also to familiarize non-medical readers, such as design engineers and operations analysts with the cause, natural history and performance impairment to be expected of each medical problem. An effort is also made to provide a substantial bibliography for workers in Clinical Space Medicine and to identify areas of research which will contribute to this field.

---

\*"a traveller in interplanetary space" (Webster's New International Dictionary, Second Edition, 1934)



This report focuses on the primary goals of Clinical Space Medicine - namely to prevent the occurrence of medical problems in space and to restore an astronaut who is suffering from a medical problem to an optimum functional capability as quickly as possible. It is conceivable, however, that an astronaut might have to forego definitive treatment temporarily while he performs a task vital to mission safety or success. During this period of time, his symptoms might be alleviated with supportive measures.

The first five chapters of this report are concerned with the various effects of decompression an astronaut could suffer. Medical problems which could result from thermal stresses are discussed in Chapters 6 and 7. Possible medical consequences of weightlessness are considered in Chapters 8, 9 and 10, and those of "particles" travelling in space in Chapters 11 and 12. Various traumatic injuries receive attention in Chapters 13 and 14. Medical problems produced by carbon dioxide, which will always be the major gaseous contaminant of space atmospheres, are reviewed in Chapter 15. Since the risks of oxygen toxicity and chronic exposure to trace atmospheric contaminants should be virtually eliminated in advanced space systems, these medical problem areas will not be discussed in this report. Finally, Chapter 16 gives consideration to the general aspects of the diagnosis and treatment of medical problems in space.

I am most grateful to Drs. A. H. Schwichtenberg, E. M. Roth and T. M. Fraser of the Department of Aerospace Medicine, The Lovelace Foundation for Medical Education and Research, for their many constructive comments which greatly assisted me in the preparation of this report. The many contributions of Dr. U. C. Luft of the Department of Physiology are also acknowledged. Gratitude is also expressed to my secretaries, Mrs. J. H. Rigler and Mrs. J. J. Whalon, and to our Chief Document Librarian, Mrs. J. Wilson, and her staff for their immense help.

D. E. B.

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## CHAPTER 1

### ACUTE HYPOXIA

A rapid unforeseen loss of the atmospheric pressure in a spacecraft cabin or space suit, leading to manifestations of acute hypoxia, possibly ebullism (Chapter 2) and explosive decompression injuries (Chapter 3), will undoubtedly always be a major hazard facing astronauts during operations in space. Any number of causes of such a critical event are conceivable. Considered foremost is penetrating damage to a space suit, possibly from contact with rugged terrain on a lunar or planetary surface, a pointed tool, a sharp projection from the spacecraft exterior, or a meteoroid. Decompression of the spacecraft cabin might result from a structural failure due to an excessive spacecraft docking or landing impact, or from penetration of a cabin wall by a meteoroid. Other possible causes of acute hypoxia include an accidental disconnect or failure of a pressure valve in a life support system, and an emergency decompression for fire extinguishment or for removal of a toxic atmospheric contaminant. Finally, acute hypoxia could result from depletion of oxygen supplied by a portable life support system, or from the purging of a spacecraft cabin atmosphere with carbon dioxide or inert gas to extinguish a fire.

In this chapter, an attempt is made to present aspects of acute hypoxia considered pertinent to the space situation. Under separate headings are discussed the sequence of clinical events which would occur during a severe acute hypoxic exposure in space, various measures which might be used in resuscitating a hypoxic astronaut, the so-called "oxygen paradox", and the characteristics and management in space of the sequelae of hypoxia - posthypoxic cerebral edema and delayed post-hypoxic encephalopathy.

#### Clinical Events in Acute Hypoxia

In their excellent review of the literature on hypoxia, Van Liere and Stickney <sup>(96)</sup> made note of the fact that all tissues of the body are immediately affected to some degree when a rapid significant reduction of

the partial pressure of inspired oxygen occurs. However the remarkable intolerance of the central nervous system, especially the brain to oxygen deprivation, accounts for the earliest and most striking manifestations of acute hypoxia <sup>(8)</sup>.

If an astronaut should suffer acute hypoxia, he could lose "useful consciousness" after a latent period of several seconds to many minutes. The term "useful consciousness" has been used to define that period during which purposeful acts can still be performed <sup>(98)</sup>. It is noted that the slower the onset of hypoxia, the more specific must be the definition of the performance degradation which reflects loss of "useful consciousness" <sup>(78)</sup>.

A hypoxic astronaut's "time of useful consciousness" will depend upon the rate of reduction and the final level of the partial pressure of oxygen in his ambient atmosphere. During this period, the astronaut should be able to function normally, so that if he recognizes the cause of a hypoxic event, he should be capable of initiating a life-saving emergency measure or declaring his situation to other members of the crew. Once beyond the "time of useful consciousness", however, he could either enter a brief "prodromal period", which is usually characterized by a high degree of helplessness, or suddenly lapse into unconsciousness.

The results of numerous decompression studies indicate that the "time of useful consciousness" of an astronaut who is rapidly decompressed to a relatively low partial pressure of oxygen should be reasonably predictable (4, 5, 7, 10, 22, 41, 66, 67, 76, 78, 101). It is noted that there is a marked variation in individual susceptibility to acute hypoxia, except at relatively high altitudes <sup>(7)</sup>. Data on the mean "times of useful consciousness" following rapid decompressions of humans who are breathing either air or oxygen throughout decompression are shown in Figure 1.1. The curves in this figure demonstrate that:

- the "time of useful consciousness" becomes shorter with increasing altitude until a minimum time is reached. From data cited by Luft (64, 66), this time appears to vary from about 10 to 15 seconds. It is reached at about 46,000 feet (106 mm Hg or 2.04 psia) when air is breathed throughout decompression,

or about 52,000 feet (79 mm Hg or 1.53 psia) when oxygen is breathed throughout decompression (93). Notably, the "time of useful consciousness" remains unchanged for decompressions above 52,000 feet whatever the concentration of oxygen in the inspired gas might be.

-below 50,000 feet, the use of pure oxygen delays the onset of unconsciousness considerably, so that in decompressions to 45,000 feet breathing oxygen, "useful consciousness" may be fully maintained for many minutes while breathing air under the same circumstances leaves little more than 10 seconds for emergency action. The difference in shape between the two curves can be attributed to the presence of nitrogen in the air-breathing decompressions.

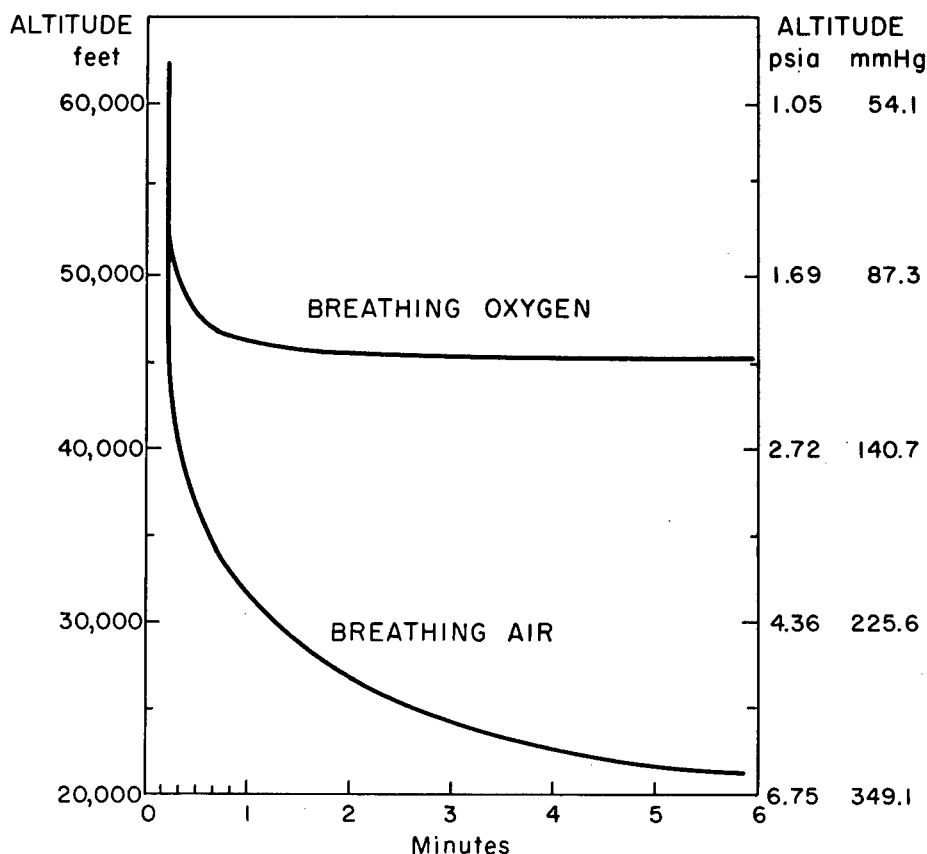


Figure 1.1 "Times of useful consciousness" on exposure to various high altitudes after rapid decompression, accomplished in less than one second, from sea level breathing 100 percent oxygen.

(After Luft (65)).

Decompression studies have also demonstrated that there is a "critical time of exposure" within which an individual must recommence breathing an adequate partial pressure of oxygen if "useful consciousness" is to be continuously preserved (3, 4, 66, 76). This time apparently also reaches a minimum with increasing altitude. Bryan and Leach (10) found that oxygen had to be given within 7 sec to subjects decompressed from 8,000 feet (564 mm Hg or 10.91 psia) to 40,000 feet (141 mm Hg or 2.72 psia) in 2.5 sec in order to preserve continuous consciousness. The average "time of useful consciousness" in their studies was 15 sec. Luft and co-workers (66), noted that the "critical time of exposure" should not exceed 5 to 6 sec in rapid decompressions (2 sec) to altitudes above 52,000 feet (79 mm Hg or 1.53 psia). Their subjects lost "useful consciousness" 15 to 17 sec after decompression.

Since the "time of useful consciousness" and the "critical time of exposure" for maintenance of consciousness of an astronaut who is rapidly decompressed to a low partial pressure of oxygen appear to be reasonably predictable, such information could be of great value if applied to the handling of unanticipated and controlled decompressions in space. If an unanticipated decompression of a space suit or spacecraft cabin should occur, an automatic emergency oxygen supply system might keep the suit or cabin pressure at a level which will not only be associated with a minimum loss of oxygen, but will also maintain "useful consciousness" for a reasonable period of time while an astronaut carries out emergency measures such as sealing a leak, returning to the spacecraft, or donning a space suit. A controlled decompression with an astronaut remaining "usefully conscious" throughout the decompression might be a practical emergency procedure under certain circumstances. For example, an astronaut might reduce his space suit pressure to give himself enough mobility to negotiate an obstacle or to release himself from a trapped situation. A controlled reduction of the cabin pressure might be used to dump into space most of an atmosphere accidentally contaminated with chemically-active particles and droplets. This measure might also be used for extinguishing a fire and, secondarily, for its cooling effect and removal of noxious fumes from the cabin

atmosphere. It must be noted, however, that rapid permanent extinguishment of a fire can be attained only by decompressing to a vacuum until the temperature of a burning system is below ignition temperature. Thus an astronaut, who will undoubtedly not have time to don a space suit prior to decompression for fire extinguishment, may experience the consequences of both hypoxia and ebullism (Chapter 2). If the spacecraft cabin atmosphere contains an inert gas, he will be subjected to a risk of decompression sickness (Chapter 4). It is assumed that if any controlled decompression produces a loss of consciousness, recompression will be programmed to occur within a time period sufficient to prevent sequelae of hypoxia and possibly ebullism.

Additional data, particularly on "time of useful consciousness", should be obtained in decompression experiments which closely simulate situations in which acute hypoxia might occur in space. Decompressions at various rates and to various partial pressures of oxygen should be carried out from anticipated space suit and spacecraft cabin atmospheres. Finally it is pointed out that "time of useful consciousness" data should be obtained on individuals performing under various work loads which could be associated with space suit operations.

Depending on the rate of the decompression and the final partial pressure of oxygen reached, loss of consciousness from hypoxia may or may not be preceded by a "prodromal period", the characteristics of which are presented below. From the decompression studies cited above, it can be concluded that unconsciousness will usually occur with startling suddenness, preceded by virtually no subjective or objective symptoms, following decompression on air to 46,000 feet (106 mm Hg or 2.04 psia) and above, or following decompressions on oxygen to 52,000 feet (79 mm Hg or 1.53 psia) and above. Occasionally, a "prodromal period", which can last about 3 sec, immediately precedes loss of consciousness following such decompressions. This relatively short period is characterized by amnesia and uncoordinated or clonic movements.

As the rate of decompression decreases or the final partial pressure

of oxygen increases, the "prodromal period" will increase in duration. The common, well documented manifestations of hypoxia at this point are predominantly due to central nervous system malfunction, characterized by aberrations of mental function, such as errors in and loss of interpretation and judgment, overconfidence, confusion, euphoria, drowsiness, paranoia and amnesia, and of neuromuscular activity, such as incoordination and clonic movements (41, 64, 67, 72).

The question arises as to whether manifestations of acute hypoxia, especially during a relatively prolonged prodromal period, could be recognized by an astronaut exposed to hypoxic conditions. If so, he might possibly be able to initiate appropriate emergency measures or signal the incident to other members of the crew. Classically, most individuals are unable to recognize subjectively any manifestations of acute hypoxia. On repeated hypoxic exposures and with adequate training, some do learn to recognize hypoxia if it comes on slowly. However, it is apparent that such a capability cannot be relied upon during operations in space, especially if hypoxia is of rapid onset or the attention of an astronaut is focused on a seemingly more important matter at the time of a hypoxic event. Therefore, even though astronauts should be well trained in this area, primary reliance will have to be placed on devices which sense and adequately warn of changes of the partial pressures of oxygen in spacecraft cabin and space suit atmospheres and, wherever possible, command the restoration of an adequate oxygen tension.

As part of a hypoxia indoctrination program, it is advisable for an astronaut to observe carefully the response of each fellow astronaut to hypoxia. Since many individuals exhibit a stereotyped response, such as euphoria, paranoia and drowsiness, to a lowered partial pressure of inspired oxygen, the knowledge of any manifestations which characterize an astronaut's response to hypoxia might be of some value in recognizing and possibly in distinguishing it from other causes of central nervous system malfunction, such as acute carbon dioxide toxicity, hypothermia and hyperthermia. Even though cyanosis is a reasonably good sign of hypoxia, this sign will be difficult to monitor visually during space suit operations. Devices which sense and warn of the occurrence

of cyanosis might be considered, but these should be ancillary to those which monitor partial pressure of atmospheric oxygen.

If exposure of an unconscious astronaut to a low partial pressure of oxygen continues, vital systems of his body will quite rapidly cease to function normally. Respiration usually fails early. Although peripheral circulatory collapse usually coincides with or soon follows cessation of respiration, some degree of cardiac activity may continue for a prolonged period of time. It is readily apparent that the times at which these events occur are related to the partial pressure of oxygen to which an individual is exposed. Data on humans from which these times might be predicted are sparse, for in human decompression experiments, exposures to low partial pressures of oxygen are stopped when consciousness is lost. Studies of prolonged accidental hypoxic events have yielded only very rough estimations of the durations of such events.

If deprived of oxygen, man has no mechanism which will enable him to survive more than a very few minutes. It is a well established fact that serious permanent damage of brain tissues begins to occur about 4 minutes after arrested cerebral circulation (84, 88). This time might be somewhat increased in cases where the cardiovascular system continues to function, and so continues to supply glucose and other nutrients to and remove toxic metabolites from the brain (19).

Cessation of respiration frequently occurred at the same time as loss of consciousness during a decompression study in which human subjects were decompressed in less than one second from 33,000 feet (196 mm Hg or 3.80 psia) to about 55,000 feet (69 mm Hg or 1.33 psia) while breathing oxygen (11). On the other hand, this event did not occur in similar studies in which individuals were exposed to altitude until consciousness was lost (3, 43, 101). If one assumes that exposure to a very low partial pressure of oxygen is essentially equivalent to a sudden circulatory arrest, respiration will cease within one minute after the exposure, cessation being preceded by stertorous periodic breathing (16, 43, 84).

It is extremely difficult to establish exact times to death for various



acute hypoxic exposures <sup>(69)</sup>. One study of hypoxic fatalities, in bomber aircrews, estimated that after onset of exposure 22 deaths apparently occurred between 5 and 15 minutes, and 4 deaths in less than 5 minutes <sup>(11)</sup>. It is noted that all these fatalities occurred at altitudes of less than 32,000 feet (206 mm Hg or 3.98 psia). Another study of 75 hypoxic fatalities at similar altitudes reported that the exact duration of exposure was known in only 6 cases, being less than 3 minutes in 4 cases and from 5 to 6 minutes in the other two <sup>(57)</sup>. Lewis and Haymaker <sup>(57)</sup> have noted that times to death appear to be much the same above certain altitudes. This may be due in part to the fact that once breathing stops, death occurs within a few minutes irrespective of the low partial pressure of oxygen to which an individual is exposed. Hence support of an astronaut's respiration would be indicated if it does not return to normal immediately after he is exposed to an adequate partial pressure of oxygen.

Events which will occur as a hypoxic individual progresses slowly through the unconscious period to death are similar to those occurring during deepening anesthesia <sup>(16, 43, 54, 84)</sup>. One who is lightly unconscious might be very difficult to manage. Restlessness, hyper-irritability and rigidity are characteristic. Convulsions and vomiting commonly occur. As unconsciousness deepens, generalized flaccidity gradually appears. Respiration becomes irregular, stertorous and finally ceases. The pupils dilate. The pulse usually responds to severe hypoxia by becoming slower. Blood pressure increases initially, then decreases as both peripheral and central circulatory mechanisms fail.

### Resuscitation

As quickly as possible, an astronaut unconscious from hypoxia must be exposed to as high a partial pressure of oxygen as can be attained. The importance of recompression as a resuscitative measure should be emphasized, particularly if a hypoxic astronaut is in a state of apnea. Recompression per se is equivalent to a deep inspiration <sup>(65)</sup>. An adequate airway must be assured by measures appropriate to the situation, such as positioning the head with the neck in extension or inserting an oral or

endotracheal airway, if these specialized techniques can be carried out in space. If breathing does not start within or remains highly irregular a few seconds after oxygen is restored, artificial respiration should be commenced, using techniques such as exhaled air ventilation or intermittent positive pressure oxygen administration by mask <sup>(75)</sup>. Most individuals breathe unassisted, if they are to survive hypoxia, within the first minute after the restoration of oxygen. Continued irregular breathing will be associated with a high probability of severe brain damage, and hence a poor prognosis for survival.

Other than the restoration of oxygen, initial resuscitative measures which might be applied to any hypoxic individual will be determined by the conditions under which the hypoxic exposure occurred and by sound clinical judgment. A vasopressor drug, such as metaraminol, might be administered parenterally if hypotension continues beyond the immediate resuscitative period. The frequent administration of sodium bicarbonate and calcium gluconate solution intravenously are also considered primary drugs for use in this situation <sup>(34)</sup>. Unless "shock" might be due in part to hypovolemia, the administration of a blood volume expander should not be required following a purely hypoxic exposure. Gordon <sup>(34)</sup> believes that the early use of an intravenous rapid-acting cardiac glycoside, such as digoxin, to improve cardiac function is contraindicated except in situations where there is definite evidence of cardiac decompensation. Of interest in this respect is the report by Webb and Haymaker <sup>(57)</sup> pointing out that pulmonary edema was one of the most common post mortem findings in fatalities from acute hypoxia at altitude (69 of 74 cases examined). Moreover, Holmstrom <sup>(42)</sup> points out that survivors of an acute hypoxic exposure at altitude not infrequently develop pulmonary edema as a serious clinical complication which requires special medical attention, particularly in cases with delayed recovery. One wonders, therefore, whether the routine prophylactic administration of an intravenous cardiac glycoside might be indicated for individuals who suffer a moderate to severe hypoxic exposure. By improving cardiac function, such a measure would combat pulmonary edema and assist in providing required rapid tissue

reoxygenation. This area does appear to require study.

Situations where resuscitative measures will be delayed, hampered and even impossible to carry out in space are easily envisaged. Other than possibly restoring an adequate partial pressure of oxygen in the space suit, artificial respiration, if required, will probably not be accomplished until the suit helmet is removed after a hypoxic astronaut is brought back into a pressurized spacecraft or airlock.

Resuscitation should be attempted on any hypoxic individual in whom there is any chance of cardiac activity or if dilated pupils respond to light, for even if his respiration has ceased, there will be no immediate indication as to how much initial irreversible brain damage has occurred <sup>(34)</sup>. The level of cardiac activity can be monitored initially by palpation especially of the carotid pulse, since it is more accessible merely by removing the space suit helmet and since other pulses, such as the radial, brachial and femoral pulses, might be inaccessible because of space suit and clothing. As well, the carotid pulse persists when the peripheral pulses are no longer palpable <sup>(34)</sup>. When possible, cardiac activity might also be monitored by cardiac auscultation, blood pressure recording and, if possible on board the spacecraft, by electrocardiography. Gordon <sup>(34)</sup> has suggested that external cardiac compression, or cardiopulmonary resuscitation be instituted if the heart is functioning but the systemic arterial pressure is under 50 mm Hg.

The duration that resuscitative measures should be carried out will also be determined by sound clinical judgment. If vital signs such as respiration, pupillary reaction to light, and response to painful stimuli do not appear and continue to improve, prognosis for survival is poor.

Depending mainly on the duration and severity of his hypoxia, an unconscious individual being resuscitated might regain full consciousness rapidly, or remain in a state characterized by impaired mental and motor function, or some level of unconsciousness, for a period of minutes to many days, or permanently. A secondary, often fatal deterioration of consciousness can occur either within hours of a hypoxic exposure without full consciousness having been regained, or within several days after a seemingly complete but prolonged recovery from a severe exposure.

These neurologic sequelae are attributed to reversible and irreversible hypoxic brain damage which results not only from the low partial pressure of oxygen at the time of exposure, but apparently also from the cerebral edema which follows severe hypoxia. Therefore, if full consciousness is not restored immediately by initial resuscitative measures discussed above, attention must be given to minimizing permanent brain damage by measures directed at cerebral edema. This is an area to be discussed below in detail.

Finally, it should be pointed out that Balke and co-workers <sup>(3)</sup> have reported that a measurable reduction in work capacity, associated with subjective symptoms of fatigue, occurred in subjects who returned to near sea level conditions after they were exposed to air at an altitude of 16,000 feet (412 mm Hg or 7.96 psia) for over 3 hours. This raises the question as to when an astronaut, who has apparently recovered completely from a hypoxic exposure, should be started back on activity associated with high work loads, unless absolutely necessary.

#### The "Oxygen Paradox"

Most individuals (about 85 percent in one series) who are still in a mildly hypoxic state can apparently experience a continued, often accelerated deterioration of consciousness for usually 15 to 30 seconds after they start breathing an adequate partial pressure of oxygen <sup>(26, 35, 55, 77)</sup>. This event is most likely to occur if pure oxygen is restored rapidly just before the onset of severe hypoxic manifestations; it is not in evidence after loss of consciousness <sup>(26, 77)</sup>. The question as to whether or not exertion or fatigue might be aggravating remains unanswered <sup>(35)</sup>.

The cause of this apparently normal reaction to reoxygenation is unknown. The temporary decrease and even cessation of breathing frequently observed on reoxygenation may promote continuance of existing cerebral hypoxia until adequately oxygenated blood reaches brain tissues <sup>(6, 35)</sup>. Constriction of cerebral vessels possibly from the hypocapnia associated with hypoxia or from elevation of the arterial oxygen tension on reoxygenation does not appear to be a mechanism involved in producing

this response to reoxygenation (77). A frequently observed, temporary vasodepressor response to reoxygenation, thought from animal studies as possibly being due to the release of a transiently-acting vasodilator substance, may contribute causally (12, 35).

A few individuals studied (2 of 180 in one series) are predisposed to suffer a severe disturbance of consciousness under the same reoxygenation circumstances as described above (77). The clinical picture presented by this truly paradoxical action of oxygen, or so-called "oxygen paradox", varies considerably between individuals, but is constant from episode to episode in the same individual (27, 77). This reaction, which usually lasts from 15 to 30 seconds in duration, is most likely to occur after exercise or a prolonged hypoxic exposure (74, 77). Typical examples of this phenomenon are a narcoleptic episode with a marked decrease of muscle tonus, an abrupt short-lasting hypertonia of skeletal muscles, an episode of peculiar hyperkineses and a sudden loss of consciousness as in an epileptic attack (77).

The cause of the "oxygen paradox" is unknown. There appears to be no characteristic physiologic or pathologic features, including narcoleptic or epileptic tendencies, which distinguish individuals prone to this reaction from those not prone (35, 77). The degree of reaction is reportedly enhanced by hyperventilation, but not significantly altered by the addition of carbon dioxide to the inspired air (77). Mechanisms mentioned for the reaction to reoxygenation discussed above may play a causative role.

Possible serious implications of the "oxygen paradox" occurring in an operational space situation are readily apparent. Accordingly, the elimination of astronaut candidates in whom this reaction can be demonstrated is considered mandatory.

### Posthypoxic Cerebral Edema

Although there has been a great deal of writing in the area of acute hypoxia in the past, only in recent years has attention been focused on the posthypoxic state and, in particular, on posthypoxic cerebral edema as

the major sequela of acute hypoxia. It has become a generally accepted fact that even though irreversible damage of brain tissues can occur at the time of an acute hypoxic event, such damage can, on occasion, be minor as compared to that caused by posthypoxic swelling, or edema of these tissues. The following discussion deals briefly with the pathophysiology, clinical manifestations, diagnosis and treatment of posthypoxic cerebral edema. Greater detail on various aspects of this syndrome is provided in reviews by Allison <sup>(1)</sup>, Cope <sup>(16)</sup>, Harley <sup>(36)</sup>, Sadove and co-workers <sup>(88)</sup>, Wyant <sup>(104)</sup>, and others <sup>(21, 61, 62, 84)</sup>.

### Pathophysiology

Edema can occur in any body tissue which is subjected to an abnormally low partial pressure of oxygen for a sufficient period of time <sup>(104)</sup>. Because of their remarkable sensitivity to a reduced oxygen supply, the brain tissues appear to be the most prone to become edematous following such an exposure <sup>(84)</sup>.

Cerebral edema has been demonstrated in experiments in which animals were subjected either to low partial pressures of oxygen or circulatory arrest <sup>(13, 23, 24, 48, 63, 99)</sup>. It was observed in about one-third of the high altitude human hypoxic fatalities reported by Lewis and Haymaker <sup>(57)</sup>. Perhaps the best indication of edema being by far the major factor in causing the posthypoxic clinical manifestations to be described below has been the clinical improvement in both animals and man resulting from the use of tissue dehydrating agents directed at reducing this edema <sup>(2, 16, 20, 32, 37, 47, 49, 73, 82, 85, 88, 89)</sup>.

Until recently, the pathophysiologic mechanisms involved in producing posthypoxic cerebral edema have been similarly stated by many investigators <sup>(16, 48, 61, 62, 84)</sup>. Hypoxia was thought to cause primarily an increase in the permeability of brain capillaries, which then allowed leakage of plasma protein from them. The consequent rise in intercellular osmotic pressure could then draw fluid out of blood vessels, leading to the formation of intercellular edema. The edema fluid would

act as a physical barrier, interfering with the passage of oxygen across the intercellular space to reversibly damaged brain cells. Intracellular edema was also thought to occur from an excessive passage of sodium and chloride ions, and hence water into cells which are functionally altered from hypoxia (16, 62, 71, 84). It was also postulated that once the cerebrospinal fluid allows for maximum expansion of the brain in its rigid bony casing, brain tissues would not only be mechanically compressed, but also have their perfusion, and hence oxygen supply diminished. Since these various effects of edema result in further hypoxic damage, the vicious circle of "hypoxia-edema-more hypoxia" would become established. The recurrence of a decreased oxygen supply could then be sufficient to inflict a final insult upon brain cells, converting reversible into irreversible damage. Thus it is understandable how brain damage, which is initially limited in degree, can assume fatal proportions or progress on to some degree of temporary or permanent decerebration of an individual when it would appear that the crisis at the time of an acute hypoxic exposure has passed.

Another mechanism might also be involved to some degree in the formation of posthypoxic cerebral edema. Studies utilizing the electron microscope have shown that glial cells in the brain swell markedly when the brain is subjected to such edema causing factors as hypoxia, hypotonic perfusion, toxic chemical agents and cold (36, 38, 44, 56, 59, 60, 79, 83). As discussed in a number of recent reviews, glial cells appear to give nutritive support to neurons and participate in the blood-brain barrier (36, 52, 68, 79, 83). The high metabolic activity associated with these and possibly other functions of glia would make these cells also highly susceptible to hypoxia, and hence would give reason for the glial edema observed after a hypoxic exposure.

It is readily apparent from the vast literature in this area that much research on hypoxia remains to be done to elucidate clearly the mechanisms involved in producing posthypoxic cerebral edema. Hopefully, such continuing research will yield optimum methods of combating this edema

therapeutically in space.

Permanent histopathologic changes in brain tissue following a hypoxic exposure have been comprehensively reviewed by Courville (18), Yant and co-workers (105), and others (40, 45). Since most of these changes are irreversible, they are not pertinent to the treatment of posthypoxic cerebral edema. It is pointed out that the majority of the clinical residues of hypoxia correlate with damage seen in the cerebral cortex, cerebellar cortex and pyramidal nuclei.

### Clinical Manifestations

Posthypoxic clinical manifestations, which have in most circumstances been attributed to cerebral edema, can vary considerably. They may appear up to several hours after either an apparently normal or a partial recovery from an acute hypoxic exposure (2, 16, 84). On the one extreme, symptoms apparently from only mild edema are experienced for a few hours (20, 97). They include headache, nausea with or without vomiting, drowsiness, emotional instability, and impairment of judgment, insight and logic. It is important to note that an astronaut in this state might be unable to perform required operational tasks.

On the other extreme is the clinical picture associated with more severe cerebral edema. It is characterized by coma, with signs depending on the depth of the coma (2, 16, 17, 49, 84, 89). Respiration may be stertorous or gasping. Pronounced sweating of the face and neck is common, and marked hyperthermia may occur early. The pupils are usually equal in size and dilated. The eyes may be open and staring, and a coarse nystagmus may be present. Restlessness, twitching movements of the limbs and actual convulsions are signs which often appear as coma deepens. Decerebrate rigidity is characteristic of deep coma. The pre-terminal events of posthypoxic cerebral edema include an increase in pulse rate, flaccidity, loss of deep tendon reflexes, hyperthermia and Cheyne-Stokes respiration.

Maximum recovery from posthypoxic cerebral edema, if left untreated,



may take hours to many days (50, 97). For some time, then, an astronaut could be a serious management problem, being unable to fulfill his own needs while in the comatose state. Even after return of consciousness, there could be a prolonged period of altered mental functioning, which could make him a potential danger to the mission or a useless member of the crew. It must also be remembered that some degree of incomplete recovery might occur. Cases of permanent hypoxic brain damage are well documented in the literature (1, 17, 18, 50, 57, 84). Coma can be permanent, with the affected individual usually dying soon from intercurrent infection or aspiration, unless rigorous supportive care is given. Residual motor involvement usually takes the form of impairment of fine coordination, spasticity or athetosis. Common mental sequelae are impairment of judgment, insight and logic, and emotional instability. It is considered reasonable to assume that any degree of permanent brain damage will affect the astronaut's highly developed skills.

It must be remembered that some degree of irreversible brain damage can occur in the pre-edematous stage of an acute hypoxic exposure. To this damage could be added that caused by cerebral edema, resulting in serious mental and motor impairment of an astronaut. It is also possible for the initial irreversible brain damage to be sufficient to produce impairment in spite of measures which might adequately control posthypoxic cerebral edema. The literature seems to support the view that if an astronaut has a severe hypoxic exposure and remains deeply comatose from the time oxygen is restored, no early decision can be given as to what his prognosis for recovery might be. A failure to respond adequately to therapy in the immediate period after a hypoxic exposure would be a strong indication of permanent brain damage.

### Diagnosis

For the most part, the diagnosis of posthypoxic cerebral edema should be obvious, especially if a deterioration of consciousness follows within a few hours what appears to be progressive recovery from an acute

hypoxic exposure. The major identifying feature of cerebral edema, if the astronaut remains in a semi-conscious or unconscious state after restoration of oxygen, will be a deterioration in his condition.

It is possible that posthypoxic cerebral edema might have to be distinguished from air embolic phenomena associated with decompression sickness (Chapter 4) or resulting from lung disruption due to explosive decompression (Chapter 3), meteoroid blast (Chapter 12), or trauma (Chapter 14). Cerebral concussion, acute subdural hematoma, and internal hemorrhage (Chapter 14), might also conceivably enter into the differential diagnosis. It is apparent that the history and physical examination, finding in particular localizing signs characteristic of the above conditions, should distinguish these conditions from posthypoxic cerebral edema. The thought should still be kept in mind, however, that as the result of a decompression event, air embolism and posthypoxic cerebral edema could occur together.

### Treatment

In the light of the foregoing discussion of the pathophysiology of posthypoxic cerebral edema, it would appear that any measure directed at breaking the vicious circle of "hypoxic-edema-more hypoxia" would be an effective form of treatment of posthypoxic cerebral edema. With this principle in mind, Sadove and co-workers<sup>(88)</sup> in 1953 reported success with dehydration therapy in humans suffering from posthypoxic cerebral edema. Their treatment entailed either repeated intravenous injections of a 50 percent glucose solution or the continuous intravenous administration of a 25 percent glucose solution. These investigators found that posthypoxic coma markedly lightened soon after each administration of hypertonic glucose. However, after a time coma returned although to a lesser depth than pre-treatment. The improvement phase was attributed to an initial net loss of water from brain tissues into the hyperosmotic intravascular compartment. The rebound phase was thought due to a rapid return of water along with glucose, which passed in excess from the intravascular compartment, so to swell the intercellular and intracellular compartments. It was thought, therefore, that agents

which are of larger molecular size and hence have a greater tendency to remain in the intravascular compartment would be more effective than hypertonic glucose in producing cerebral dehydration. Several more effective agents suggested were concentrated human serum albumin, plasma expanders such as dextran and polyvinylpyrrolidone and quadruple-concentrated plasma.

In the past 14 years, a number of dehydrating agents, or so-called osmotic diuretics, have been used successfully in the treatment of posthypoxic cerebral edema. Experiments on animals have shown that urea and mannitol are effective in decreasing brain volume, increasing cerebral blood flow, decreasing cerebrospinal fluid pressure, and producing clinical improvement of this syndrome (9, 13, 32, 33, 37, 47, 73, 82, 102). Success in treating humans has been reported for sucrose, albumin, urea and mannitol (2, 16, 51, 81, 84, 85, 89, 90). Of all the dehydrating agents used in the past, mannitol would appear to be the most appropriate for the treatment of posthypoxic cerebral edema in space. In animal and human experiments, which studied the cerebrospinal fluid pressure responses to intravenous equimolar doses of hypertonic urea and mannitol, it has been shown that urea produces a greater decline of this pressure, but the mannitol effect lasts longer (73, 82, 91, 102). Furthermore, it was noted that although a secondary rise of cerebrospinal fluid pressure occurred after the administration of both of these agents, this rebound effect was much greater with urea. These findings correlate well with human clinical results, for mannitol appears to be not only more effective than urea and other dehydrating agents mentioned above in reducing the cerebral edema, but is also much less likely to produce rebound (48, 51, 84, 85). The clinical usefulness of mannitol has been attributed to the fact that it possesses the many properties desirable for a dehydrating agent, for it is non-toxic, is not significantly metabolized or stored in the body, remains almost entirely outside of the intracellular compartment, and is excreted rapidly by the kidneys (21, 25, 85, 91, 102). Since mannitol is not reabsorbed in significant amounts from the renal tubules, it acts as an osmotic diuretic. This characteristic accounts for the well

known usefulness of this drug in preventing acute renal tubular necrosis from a variety of causes. A practical advantage of mannitol is the fact that it is easily dissolved in the concentration recommended for injection. Therefore, it is apparent that a strong case can be made for using mannitol in the treatment of posthypoxic cerebral edema in space. However, this view must be substantiated as this drug receives greater clinical usage with time.

Mannitol is administered in various concentrations (e.g., 20 percent solution) only by the intravenous route. Doses of up to 200 gm spread over a 24 hour period have been used safely (39, 51). Because of the high urinary output which will accompany the administration of this agent to a comatose astronaut, his urinary bladder should be catheterized.

What should be the indication for and the time of administration of a cerebral dehydrating agent to an astronaut who has suffered an acute hypoxic exposure? From past experience, it appears that cerebral edema should be assumed responsible for some of the neurologic manifestations which occur up to several hours after exposure. Theoretically and clinically, a dehydrating agent should be administered for both preventive and therapeutic purposes. Such an agent should be given to an astronaut, who shows an inadequate neurologic response to oxygen, as soon as there is clinical evidence of adequate cardiovascular function.

Hypothermia has been markedly effective when used experimentally for the treatment of posthypoxic cerebral edema in animals (9, 85, 103, 106). This measure, usually combined with dehydration therapy, has reportedly been highly beneficial in treating this syndrome in humans (36, 61, 84, 88, 89, 95, 100, 103). Reasons for its efficacy, as given by Harley (36) and Wolfe (104), center on the improved balance between oxygen availability and demand in cooled, edematous brain tissues. Hyperpyrexia, which in itself can produce permanent brain damage, is prevented. Even in normal individuals, hypothermia reduces brain volume and intracranial pressure (27). Thus, according to the more

recent concept of the cause of posthypoxic cerebral edema, hypothermia minimizes damage of brain elements, including the glial cells, and any associated edema.

The level of hypothermia recommended for the treatment of posthypoxic cerebral edema has been between 30° C (86° F) and 32° C (89.6° F) (36, 104). The importance of controlling shivering, which can detrimentally increase cerebral oxygen consumption, has been emphasized (36). As is used even today, suppression of shivering would be possible with chlorpromazine.

Although hypothermia would apparently be of great value in the treatment of posthypoxic cerebral edema in space, therapeutic hypothermia might be operationally impossible in the foreseeable future. It is conceivable, however, that adequate total body cooling might be attained with a water-cooled space suit.

Finally, it should be mentioned that corticosteroids and corticosteroid-antihistamine combinations have been employed with great success in the relief of the edema and signs and symptoms associated with brain tumors (14, 28, 30, 31, 44, 53, 58, 70). In animal studies, these agents have also reduced edema of cerebral tissues induced by toxic agents and cold (60, 87, 94). Such drugs appear to combat edema formation primarily by reducing capillary leakage. However, their value in the treatment of posthypoxic cerebral edema remains to be determined.

Various supportive measures are required in treating an astronaut who is suffering from posthypoxic cerebral edema. Measures to assure adequate oxygenation may include continuing his exposure to 100 percent oxygen, assisting his ventilation, maintaining a clear airway by measures mentioned above, and removing secretions from his respiratory tract. Provided there is no chance of serious respiratory depression, a sedative such as sodium phenobarbital might be required for controlling mental and motor manifestations, including convulsions, associated with posthypoxic cerebral edema. An oral or systemic tran-

quilizing drug, such as chlorpromazine, might also be of benefit in this situation. Intravenous fluids and electrolytes might be needed not only for feeding a comatose astronaut, but also for restoring his blood volume and electrolyte losses if dehydration therapy is carried out. Since gastric dilatation often accompanies the onset of cerebral edema, oral feeding should be withheld for the immediate posthypoxic period. Nasogastric intubation might be required for relieving this condition; it can also be used for feeding a comatose astronaut. Catheterization of the urinary bladder might be required, especially if a cerebral dehydrating agent is administered. A broad spectrum antibiotic might be given prophylactically for secondary respiratory and urinary tract infection if the period of coma is prolonged.

#### Delayed Posthypoxic Encephalopathy

Delayed posthypoxic encephalopathy is a serious neurologic deterioration which occurs several days following a seemingly normal clinical recovery from an acute hypoxic exposure. This problem is fortunately a very rare consequence of acute hypoxia, for Shillito and co-workers<sup>(92)</sup> discovered that only 13 cases of delayed posthypoxic encephalopathy occurred in 21,000 cases of carbon monoxide poisoning. Hence it will only be briefly discussed here.

A clear clinical picture of delayed posthypoxic encephalopathy has been presented in reviews by Plum<sup>(80)</sup> and Shillito<sup>(92)</sup> and their respective co-workers. The hypoxic exposure is usually severe, with most individuals awakening from posthypoxic coma within 24 hours and resuming full activity in 4 or 5 days. A clinically normal period of 2 to 10 days, and occasionally longer, follows. Then, abruptly, these individuals become irritable, apathetic, and confused. Some are agitated or manic. Motor control is usually clumsy, and diffuse skeletal muscle spasticity may develop. This neurologic deterioration may progress to coma and death, or be arrested at any level. Some individuals

recover to full health over a period of many months.

Extensive cerebral hemispheric demyelination, with no predilection for perivascular regions, appears to be the major pathologic abnormality common to all cases of delayed posthypoxic encephalopathy. Cerebral edema or swelling is absent as is damage to nerve cell bodies and axons.

The cause of this condition is not known. Although cerebral demyelination has followed hypoxia in several experimental studies, this paradox of extensive demyelination coupled with neuronal preservation has rarely been seen in such studies <sup>(80)</sup>. Recent findings would support the hypothesis that injury to the glia, which appear to be not only involved in the production and maintenance of myelin but also highly sensitive to oxygen lack, are responsible for this delayed consequence of hypoxia <sup>(36, 68)</sup>.

Unfortunately there are no clinical signs which predict delayed posthypoxic encephalopathy before it occurs. The history of a hypoxic exposure and the diffuse findings with long latency described above should distinguish this syndrome from other conditions, such as psychiatric disease and chronic subdural hematoma.

Since the etiology of posthypoxic cerebral encephalopathy is unknown, it is possible to make no more than empirical suggestions for its treatment. This syndrome appears to occur for no defined reason after an individual recovers and resumes full activity after a severe hypoxic exposure, so that it might be wise to restrict the physical activity of an astronaut in such a situation as much as possible for many days. Once neurologic deterioration occurs, only the supportive forms of therapy discussed previously for posthypoxic cerebral edema can be suggested at this time.

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## CHAPTER 2

### EBULLISM SYNDROME

Especially during extravehicular operations in space, astronauts will risk accidental exposure to an ambient pressure which is equal to or less than the effective vapor pressure of body fluids at body temperature. Such an exposure will lead to profuse evaporation and outgassing of these fluids, with the formation of vapor bubbles in tissues, blood vessels and body cavities. This phenomenon has been termed "ebullism" and its resulting clinical manifestations, the "ebullism syndrome" (22, (26). For all practical purposes, ebullism can be expected to occur at ambient pressures of 47 mm Hg (63,000 ft) or less.

It must be kept in mind that an astronaut subjected to ebullism will also suffer from primary acute anoxia (Chapter 1). Moreover, injuries sustained during an "explosive" decompression (Chapter 3) could further complicate the clinical picture of an astronaut who has experienced a decompression event.

A discussion of the pathophysiology, clinical manifestations, diagnosis and treatment of the ebullism syndrome follows. For more detailed information on the general aspects of this syndrome, including the results of animal experimentation in this area, reference is made to a recent monograph by Roth (22). Also pertinent are reviews by Luft (20), Ward (26), and others (2, 16, 28).

#### Pathophysiology

The ebullism syndrome as it could occur in an astronaut has not been described for man. Moreover, only in the past few years have manned orbital flights and the increasing use of man-rated space simulators necessitated experiments exposing animals to "space" in order to predict with a reasonable degree of confidence what effects such an exposure could have on astronauts (3, 4, 5, 7, 8, 9, 10, 11, 12, 18, 24). There appears to be no reason to suggest why the results of such experi-



ments, particularly those with large primates, should not be reasonably but cautiously extrapolated to man.

Animal experiments have shown that ebullism does not occur uniformly throughout the body (7, 20, 23). Vaporization and outgassing tend to occur at various places in the body, depending on such local factors as temperature, hydrostatic pressure, tissue elasticity, solute concentration, and the presence of gas nuclei (17). These factors account for the early appearance of vapor bubbles at or even slightly above a total ambient atmospheric pressure of 47 mm Hg in sites such as the pleural cavity and in the large central venous channels. In the former site, the pressure is usually less than that of the ambient atmosphere and in the latter site, the hydrostatic pressure is minimum and temperature of the blood is maximum (11, 13, 17). As would be expected, profuse vaporization from the warm moist membranes of the respiratory passages and ocular conjunctivae occurs at a total ambient pressure close to 47 mm Hg (11).

The most significant pathophysiologic events observed during ebullism appear to result from bubble formation within the cardiovascular system. Almost immediately after decompression to an ambient atmospheric pressure at which ebullism can occur, vapor bubbles form at the entrance of the great veins into the heart (7, 13). Vaporization then rapidly progresses in a retrograde fashion through the venous system to the capillary level. Venous return is blocked by this "vascular vapor lock". This leads to a precipitous fall in cardiac output, a simultaneous reduction of the systemic arterial pressure, and the development of vapor bubbles in the arterial system and in the heart itself, including the coronary arteries (7, 15, 20). Systemic arterial and venous pressures then approach equilibrium with that of water vapor (9). Animal studies have demonstrated that the circulation virtually ceases completely within 10 to 15 seconds after explosive decompression to an ambient atmospheric pressure of 30 to 40 mm Hg and within 10 seconds after rapid decompression to near-vacuum (9, 10, 15). Interestingly, these cardiovascular effects of ebullism contrast with the cardiovascular

effects of profound acute hypoxia per se, in that the cardiovascular pressure response to hypoxia is manifested by a transient fall in systemic arterial blood pressure followed by a rebound, then a gradual decline over several minutes due to hypoxic circulatory failure <sup>(14)</sup>. Hence the pathologic effect of ebullism, particularly on brain tissues, might be even more severe than the effect of profound acute hypoxia per se, for if cardiovascular ebullism occurs, the tissues will be deprived not only of oxygen but also of the supply of other circulating nutrients such as glucose and the removal of toxic metabolites such as carbon dioxide and lactic acid <sup>(27)</sup>.

During an ebullism exposure, cardiac damage might result from stretching of the myocardium by expanding gas inside the heart, combined with the effects of fulminating anoxia <sup>(7)</sup>. These factors were cited to explain the markedly abnormal cardiac electrical activity frequently observed in dogs explosively decompressed to an ambient atmospheric pressure of 30 mm Hg, and the failure to resuscitate the dogs so exposed for over 3 minutes in duration <sup>(7)</sup>. They might also have been involved in producing the fatal cardiac arrhythmias observed in other animal exposures to near-vacuum <sup>(3, 4, 5, 9, 19, 24)</sup>.

Profuse fluid vaporization from the moist membranes in the respiratory tract apparently can traumatize delicate lung tissues <sup>(3)</sup>. Water vapor, oxygen, carbon dioxide and nitrogen or other inert gases, if present in the atmosphere prior to decompression, pour out of the pulmonary blood and tissues and rapidly escape through the airways into the surrounding environment. Whether the widespread pulmonary edema, atelectasis, congestion and hemorrhage observed in animals following ebullism are due to a disruptive effect of escaping gases, to tissue cold injury from fluid vaporization or to some combination of these factors has not been determined. The severity of lung damage does increase with the rate of decompression and the duration of the ebullism exposure <sup>(3)</sup>. Interestingly, serious lung damage was not observed in dogs subjected to near-vacuum unless their exposure time exceeded 90 seconds <sup>(11, 12)</sup>. Denitrogenation, or the breathing of oxygen for a period of time prior to exposure also exercised a significant protective effect on the degree

of lung involvement (4, 5, 11, 12). Finally, it is noted that the atelectasis observed in animals exposed to total ambient atmospheric pressures at which ebullism occurred might in part be attributed to a displacement of intra-alveolar gasses by fluid vapor, followed by collapse of vapor-filled spaces on recompression (20). The vapor which forms in the pleural "space", and so partially collapses the lung, might also be an important factor in producing atelectasis (14).

Heat losses mainly from fluid vaporization in the respiratory tract and on the skin surface has diminished the lower esophageal temperature of animals decompressed to near-vacuum for survivable lengths of time by several degrees centigrade (9). Lowered body temperature reduces the vapor pressure of body fluids as well as tissue metabolism. However it is not known whether this phenomenon would affect survival. No doubt the body cooling takes place mostly within the chest and at the skin surface. Because of cardiovascular vapor lock, cooled blood cannot circulate to highly oxygen-sensitive brain tissues until brain perfusion is restored after recompression. Since this blood would be an admixture of blood from cooled and uncooled parts of the body, it would probably not be cool enough to confer significant protection from hypoxia on brain tissues between the moment of recompression and the restoration of adequate brain tissue oxygenation. Finally, whether blood cooling from ebullism could ever be great enough in a human to produce fatal ventricular fibrillation (Chapter 7) remains to be determined.

Vaporization and outgassing at sites in the body other than those mentioned above appear to be of minor pathophysiologic significance. Projectile vomiting, defecation, lacrimation, salivation, and urination have been observed in animals at the time of exposure to ambient atmospheric pressures at which ebullism occurred (3, 4, 5, 7, 8, 13, 14, 15, 17, 18, 24)

Most important from a clinical standpoint in the ebullism syndrome appears to be the consequences of the profound anoxic exposure combined with the damaging effects of intravascular, and possibly extravascular bubbles which might fail to reabsorb completely coincident with recompression. Roth (23) summarized his discussion of the dynamics of subcutaneous vapor pockets forming in ebullism by stating that there is first

a rapid conversion of liquid water to the vapor phase. This phenomenon reaches a peak rate at about one minute and then probably continues on at a slower rate for several minutes. He noted that there is an original rush of carbon dioxide, nitrogen, and oxygen into the pocket, but that carbon dioxide gradually becomes the most abundant gas. Reference was made to the pressure data of Kempf and co-workers <sup>(17)</sup>, who showed that by 60 seconds after decompression to an ambient atmospheric pressure at which ebullism occurs, these gases may make up to about 10 percent of the total pressure within subcutaneous vapor bubbles. If it is assumed that the diffusion of gases into and out of vapor bubbles within the cardiovascular system approximates the diffusion of gases into and out of subcutaneous vapor bubbles, then there is a likelihood that some intravascular bubbles might fail to reabsorb completely on recompression, especially if the pre-decompression ambient atmosphere contains an inert gas. The probability of this occurring will increase with the length of time that ebullism is experienced. These post-ebullism bubbles could then continue to act as emboli, and so inflict temporary and possibly permanent tissue damage. By blocking blood flow through such critical tissues as the heart, brain, and lungs, they could conceivably be the major contributor to post-recompression death.

The rate of decay of a post-ebullism bubble is determined by the same factors which control the rate of reabsorption of a bubble of decompression sickness (Chapter 4). Complicated theoretical considerations beyond the scope of this discussion indicate that post-ebullism bubbles will always contain higher levels of carbon dioxide and oxygen than inert gas, and hence should reabsorb much more rapidly than bubbles of decompression sickness <sup>(22)</sup>. It is noted that the rate of reabsorption of a post-ebullism bubble will vary inversely with the amount of inert gas in the bubble, and hence on the duration of the decompression exposure. Roth <sup>(22)</sup> has discussed the significance of various inert gases in the reabsorption of post-ebullism bubbles. He concluded that because of its low permeation coefficient in blood, neon in a bubble would be reabsorbed more rapidly and therefore would be a "safer" inert gas for an astronaut to have in his ambient atmosphere than nitrogen. It was also postulated that nitrogen

would be a "safer" gas than helium. He predicted, however, that the overall dependence of the ebullism syndrome on the type of inert gas used would be much less for this syndrome than for decompression sickness. The observation that animals recover less rapidly after a brief exposure to a total ambient pressure at which ebullism occurs than after a decompression episode at a partial pressure just below this level has been attributed primarily to the existence of post-ebullism bubbles <sup>(20)</sup>.

The recovery of dogs, squirrel monkeys, and chimpanzees has been studied after their exposure to near-vacuum for varying periods of time <sup>(3, 4, 5, 7, 8, 9, 10, 18, 19, 24)</sup>. Perhaps the experimental observations which might best be extrapolated to man are those on chimpanzees <sup>(18, 19)</sup>. However, when extrapolating the following experimental observations to man it must be kept in mind that the functional capabilities of man are much higher than the chimpanzee. Thus man might suffer a severe loss of higher psychomotor functions with a degree of brain damage which would still allow a chimpanzee to function adequately. Several chimpanzees, denitrogenated by breathing pure oxygen for four hours prior to decompression, have tolerated exposures to ambient atmospheric pressures of less than 2 mm Hg for up to 210 seconds with a return of apparently normal psychophysiologic function after recompression. Manifestations during the period of recovery are not unlike those during a recovery from a severe acute hypoxic episode. The time for first purposeful movement to occur after recompression increases with the duration of exposure, being about five minutes for a 60 second exposure, 20 minutes for a 120 second exposure, and 40 minutes for a 150, 180 and 210 second exposures. Likewise, the time for apparently complete recovery of normal psychomotor functioning after recompression increases with the time of exposure, being about 90 minutes for a 60 second exposure and less than four hours for 120, 150, 180 and 210 second exposures. From the time of first purposeful movement until recovery, these chimpanzees demonstrated varying degrees of confusion, lag time in task performance, diminished perception of auditory and visual stimuli, and motor incoordination and rigidity. Whether or not personality changes could occur and persist for varying periods of time, or even permanently, after recovery from the more prolonged exposures

remains to be determined. It is apparent that such experiments must be carried out on a larger population, extending the duration of exposure beyond 210 seconds before a more complete picture of all the possible manifestations, both temporary and permanent, of the ebullism syndrome can be presented for the chimpanzee. If spacecraft cabin atmospheres are to contain inert gas, then these primates should also be decompressed while breathing such atmospheres in order to determine inert gas contribution to clinical effects which, as noted above, could be markedly augmented in such a situation by post-ebullism bubbles.

Experiments with animal species other than the chimpanzee would suggest that when an astronaut experiences ebullism beyond 150 seconds in duration, the period of temporary functional impairment will be increasingly prolonged and manifestations of permanent brain damage will appear and rapidly increase in severity, especially if the astronaut is decompressed from an atmosphere containing inert gas (3, 4, 5). From autopsies on animals which did not survive ebullism and observation of animals which recovered, it appears that brain damage in the ebullism syndrome is more diffuse than focal in nature. Cerebral edema (Chapter 1) resulting from the combined effects of the acute anoxic exposure and under certain circumstances brain tissue hypoxia secondary to blockage of cerebral vessels by post-ebullism bubbles will no doubt play the major role in the production of temporary and permanent cerebral manifestations of the ebullism syndrome. Finally there is experimental evidence that one or more post-ebullism bubbles can produce nervous tissue damage of a more focal nature. One dog subjected to ebullism exhibited severe post-decompression paralysis which gradually recovered over a period of weeks (3, 4, 5). Its spinal cord had numerous demyelinated lesions which seemed to be the result of gas bubble emboli (11, 12). Another dog manifested severe post-decompression paralysis which slowly improved over a two month observation period. This time focal lesions were found in both the brain and spinal cord, especially in their white matter (8). The predilection of white matter for such damage may be due to the fact that as compared to gray matter, it is not only less vascular but also has a greater solubility for nitrogen (8). Intra- and possibly extravascular, or autochthonous

bubble formation have both been implicated in the production of this pathology.

Blockage of coronary arterial blood flow in an astronaut is considered a serious possible consequence of post-ebullism bubbles. Due to the cumulative effects of an inadequate myocardial blood supply, impaired cardiac function could manifest itself immediately after recompression, or from minutes to many hours thereafter. Permanent myocardial damage leading to some degree of chronic myocardial insufficiency might even be possible.

It is conceivable that by depriving vascular beds of an adequate blood supply, ebullism bubbles could produce such wide-spread vascular injury, leading to impaired vasomotor control and loss of plasma through damaged capillary walls, that circulatory collapse might occur. As in decompression sickness (Chapter 4), this might occur up to several hours after recompression. Myocardial insufficiency secondary to bubble emboli might or might not assist in producing "shock". As in decompression sickness, the lungs could well be the main site of this plasma loss, especially since vapor bubbles tend to form in the right side of the heart. Animals autopsied after ebullism have demonstrated marked pulmonary edema. The observations that the pulmonary edema is much less severe, and is associated with a lower mortality rate in those animals which denitrogenated as compared to those that breathe air prior to decompression lend support for the prediction on the theory that inert gas can play a detrimental role in the ebullism syndrome (11, 12, 22).

#### Clinical Manifestations

The fact that the ebullism syndrome has not been described to date for man bears re-emphasis. Moreover, animal experimentation has yielded data for near-vacuum exposures lasting up to only 210 seconds. Therefore the predicted clinical manifestations of the ebullism syndrome in man must be based not only on such data but also, for exposures longer than 210 seconds, on theoretical considerations.

From the discussion of man's clinical response to acute hypoxia in Chapter 1, it is apparent that if an astronaut is suddenly exposed to an

ambient atmospheric pressure at which ebullism will occur, time of useful consciousness will be about 10 to 15 seconds. As shown in ebullism experiments, and also pointed out in Chapter 1, hypoxic manifestations should not appear if, after a one second or less time to altitude, recompression is accomplished within 4 to 5 seconds' of exposure (4, 5).

Loss of consciousness will be abrupt. The ensuing state of flaccid paralysis might be preceded by tonic and clonic seizures lasting up to several seconds in duration. Systemic arterial pressure will fall precipitously, probably within 15 seconds after decompression. Breathing will be arrested about the time consciousness is lost or within a few seconds thereafter.

Marked abdominal distension will occur immediately after being decompressed, and possibly promote vomiting, defecation and urination, which could create an extremely serious particle and droplet hazard in the weightless environment if the exposure is survived (Chapter 9). A striking swelling of the subcutaneous tissues, beginning in loose skin areas such as the eyelids, axillae, scrotum, and neck will be noticeable within 10 seconds after decompression. As exposure continues beyond this time, this swelling will extend rapidly, creeping into some adjacent areas and extending rapidly into others. Since man's skin is "tighter" than the skin of animals, it is likely that this swelling will be much less in humans than that seen in animal exposures.

In general, the rate of recovery of an astronaut after suffering the effects of ebullism will be determined by such factors as the duration of his decompression, the rate of recompression and whether or not air or oxygen is breathed during recompression. As might be expected, the shorter the exposure and the faster the rate recompression while breathing oxygen, the greater and less complicated the recovery of animals subjected to near-vacuum (4, 5).

If a recompressed astronaut survives the immediate effects of ebullism and resuscitative measures are not employed, it might take up to a minute or more for adequate respiration to return, depending on the duration of his decompression. Recompression will in essence be a first



breath. If an astronaut is recompressed with oxygen there need not be an urgent requirement for artificial respiration, for adequate apneic oxygenation of pulmonary blood can occur for a period of time without interference from carbon dioxide accumulation providing, of course, his airways are unobstructed. Respiration might remain irregular for several minutes. If longer, the probability of severe temporary and possibly permanent brain damage will be great.

A recompressed astronaut's cardiovascular function might also take up to several minutes to return to an adequate level. Failure to do so might be due mainly to myocardial insufficiency caused by bubble embolization to the coronary arteries. This clinical state is characterized by a persistent tachycardia, arterial hypotension and venous distension. As mentioned previously, impaired vasomotor control and plasma loss might conceivably contribute significantly to the production of circulatory collapse, which might occur up to several hours after recompression and possibly have fatal consequences.

If an astronaut who is suffering from the ebullism syndrome does not have the benefit of therapeutic measures other than recompression, his time to maximum recovery might take hours to days and even weeks. Since it is thought that prolongation of recovery would be due to cerebral edema, the psychomotor manifestations which an astronaut will present will be much the same as those described for post-hypoxic cerebral edema (Chapter 1). Although considered more unlikely following ebullism, focal reversible or irreversible damage of brain tissues might occur, the clinical picture from this being thought essentially the same as that described for decompression sickness (Chapter 4).

Finally it is considered possible that pulmonary atelectasis secondary to ebullism could be severe enough to produce inadequate pulmonary ventilation. This problem would be characterized by rapid shallow breathing and persistent cyanosis. Hypoxia and carbon dioxide retention secondary to atelectasis might lead to death. Persistent atelectasis favors pulmonary

infection, which could seriously complicate an astronaut's recovery from ebullism.

### Diagnosis

The diagnosis of ebullism itself should be obvious. However certain manifestations of the ebullism syndrome which occur after recompression might only be diagnosed by history, physical examination, and the use of special diagnostic procedures. The crepitus of subcutaneous bubbles might possibly be felt after recompression in a surviving case of prolonged exposure. Deepening unconsciousness, prolonged unconsciousness or delayed deterioration of consciousness after recompressing an astronaut might be indicative of either cerebral edema or cardiovascular "shock". Tachycardia, arterial hypotension and venous distension might be diagnostic of cardiac failure. Rapid shallow breathing and persistent cyanosis might represent pulmonary atelectasis. If possible on-board the spacecraft, a hematocrit determination could be used to diagnose pulmonary atelectasis.

### Treatment

Up to the present time, the treatment of the ebullism syndrome has not received attention. Experimentation is certainly warranted in this area to justify the use of specific therapeutic measures which are indicated by theoretical considerations. In addition, a number of resuscitative supportive measures should be available and administered as sound clinical judgment dictates.

The initial resuscitative measures which might be applied to an astronaut who has suffered ebullism are similar to those discussed in detail under acute hypoxia in Chapter 1. He should be exposed to as high a partial pressure of oxygen as possible. However, in order to minimize the risk of pulmonary atelectasis which accompanies the use of 100 percent oxygen at reduced pressures, it might be wise to switch him to an inert gas-oxygen mixture as soon as his cyanosis clears.

From theoretical considerations, it is conceivable that immediate recompression of an astronaut to hyperbaric levels to hasten the reab-

sorption of post-ebullism bubbles might be a highly effective measure in the treatment of the ebullism syndrome. The rationale of having a recompression facility available for the treatment of this syndrome as well as decompression sickness and other air embolic phenomena which might occur during space operations is discussed under the treatment of decompression sickness in Chapter 4. If an astronaut can be recompressed, it is thought that due to the relatively lower inert gas content of post-ebullism bubbles, an adequate clinical result might be attained at an even lower ambient pressure in the treatment of ebullism than in the treatment of decompression sickness. This will particularly be so if ebullism results from decompression of the space suit, for an astronaut will be breathing 100 percent oxygen and so releasing the inert gas of the spacecraft cabin atmosphere from his body tissues for a period of time before his ebullism exposure. Since the lower the partial pressure of nitrogen in the inspired gas, the greater is the reabsorption rate of bubbles which contain nitrogen, it would seem advisable to have an astronaut breathing 100 percent oxygen or another inert gas throughout the period of his hyperbaric recompression <sup>(14)</sup>. On the other hand, the tendency of a pure oxygen environment to produce pulmonary atelectasis must be kept in mind. It is noted that if 100 percent oxygen is breathed, the recompression pressure would have to be limited to the lower pressure range (up to 3 atmospheres absolute) to prevent oxygen toxicity.

Positioning a recompressed astronaut in the head-down, left lateral position to minimize the migration of air emboli into the coronary and brain vessels will obviously be of no therapeutic benefit in the weightless environment. This measure should be carried out, however, if ebullism has occurred under sub-gravity conditions. If manifestations of pulmonary atelectasis are in evidence, reinflation of his lungs should be attempted. Mouth-to-mouth breathing or intermittent positive pressure oxygen are suitable means by which this might be accomplished initially. If he is conscious and if residual pulmonary atelectasis is found still to be present, he might continue periodic pressure breathing or be encouraged to cough or breathe deeply at intervals.

An astronaut suffering from the ebullism syndrome who does not respond adequately to oxygen should be treated for cerebral edema according to the indications and measures discussed under post-hypoxic cerebral edema in Chapter 1. If undertaken, dehydration therapy should begin as soon as possible after his systemic arterial pressure is restored to an adequate level. Because of myocardial infarction and plasma loss, this factor may be more critical in the therapy of ebullism than in post-hypoxia per se.

Various forms of supportive therapy should be administered as indicated. An intravenous vasopressor, such as metaraminol, and a rapid-acting intravenous cardiac glycoside, such as digoxin, might be given until the systemic arterial pressure stabilizes. The cardiac glycoside might be continued indefinitely if it appears that myocardial damage has occurred. Other intravenous fluids might be given not only for the feeding of an unconscious or semiconscious astronaut, but also for restoring excessive fluid and electrolyte losses from dehydration therapy. Such fluids must be given with care if myocardial damage has occurred.

The question as to whether a pulmonary vasodilator could provide some relief of the clinical manifestations produced by post-ebullism bubbles trapped in the pulmonary circulation remains to be answered. Such an effect would depend to some degree on the ability of such a drug to release the vascular spasm at sites of bubble lodgment. Isoproterenol would be the drug of choice, not only for its pulmonary vasodilatory activity, but also for its positive inotropic and chronotropic actions (1, 6). Since metaraminol is a pulmonary vasoconstrictor, the administration of this drug to restore systemic arterial pressure in this situation is debatable (1). On the one hand, it might tend to counteract the effect of a pulmonary vasodilator or if a vasodilator is not given, might seriously jeopardize pulmonary blood flow already partially blocked by bubbles. On the other hand, metaraminol might have no further effect on pulmonary vessels already maximally vasoconstricted due to bubbles. Experimentation in this area therefore appears indicated.

Sedation with a drug, such as phenobarbital, might be required for controlling mental and motor manifestations, including convulsions, of the ebullism syndrome. Since gastric dilatation often accompanies cerebral edema, oral feeding should not be attempted in the immediate post-recompression period. Nasogastric intubation may be needed for relieving gastric dilatation and used later if required for feeding. Urinary bladder catheterization should be undertaken if an astronaut is semicomatose or comatose. Prophylactic antibiotic therapy should be rendered if some degree of pulmonary atelectasis persists or if an astronaut remains in coma for a prolonged period of time.

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### CHAPTER 3

#### "EXPLOSIVE"\* DECOMPRESSION INJURIES

However remote the possibility might be, astronauts will always face the potential hazard of "explosive" decompression during space missions. Such an extremely rapid reduction of the ambient atmospheric pressure of a spacecraft cabin might be caused by penetration of the cabin wall by a large meteoroid or structural failure resulting from a landing accident on a moon or planet. The space suit might be accidentally perforated by accidental contact with sharp stationary objects or with tools and other movable extravehicular equipment during extravehicular operations.

Theoretical analyses of "explosive" decompression transients have been presented by Haber and Clamann (8) and others (12, 13, 15). These analyses indicate that the possible injuries from an "explosive" decompression are determined by the change in absolute pressure, the ratio of the initial to the final ambient atmospheric pressure and the rate of decompression. It is important to remember that one of the main factors which determines the rate of decompression is the ratio of the volume (V) of the spacecraft or space suit to the effective area (A) of the decompression orifice. This ratio becomes the time characteristic ( $t_c$ ) of decompression when the velocity of sound (C) is included in the relationship

$$t_c = \frac{V}{A \cdot C}$$

for the particular volume and decompression orifice under consideration. It is noted that the time characteristic is independent of pressure.

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\*It is noted that for thermodynamic reasons, the flow of gases through an opening in the spacecraft cabin wall or in the space suit cannot exceed the speed of sound. On the other hand, one of the physical characteristics of an explosion is that its air blast is supersonic. Therefore the term "explosive" decompression is actually a misnomer. However, it is commonly used to refer to extremely rapid decompressions occurring in less than one second (2).

During "explosive" decompression, an exposed astronaut might sustain injuries inflicted internally by the rapid expansion of gases in gas-containing organs such as the lungs. A variety of mechanical injuries (Chapter 14) might be inflicted externally not only by being displaced or being struck by displaced objects as the cabin air rushes toward the decompression orifice, but also by the factor causing the decompression. After "explosive" decompression, acute hypoxia (Chapter 1) and ebullism (Chapter 2) will probably be experienced.

This chapter is mainly concerned with the pathophysiology, clinical manifestations, diagnosis and treatment in space of possible internally inflicted, "explosive" decompression injuries. The most likely externally inflicted injuries are mentioned, but discussion of their treatment is reserved for Chapter 14.

### Internally Inflicted Injuries

#### Pathophysiology

Since the solid and liquid constituents of the body are not deformed by changes of ambient atmospheric pressure, only those organs which contain appreciable amounts of free gas are immediately affected by "explosive" decompression. Whenever expanding intracorporeal gases cannot readily escape during an "explosive" decompression, they will exert pressure on surrounding tissues. Due to their fragile structure and the large amount of gas they contain, the lungs are more susceptible to injury by overpressure than the abdominal organs <sup>(13)</sup>.

It has been established experimentally that if the intact mammalian lung-thorax system is permitted to expand passively, lung structure will disrupt at pressure differentials across the lungs and chest wall of about 80 mm Hg <sup>(1, 17)</sup>. This is in contrast to the pressure differentials of more than 150 mm Hg frequently tolerated in the act of coughing, during which active muscular effort actually reduces lung volume by compressing its gas content <sup>(13)</sup>.

Fortunately the probability that an astronaut's respiratory passages

could be obstructed and hence overdistended by trapped intrapulmonary gases at the instant of an "explosive" decompression is very remote. Moreover, it appears that patent airways will allow adequate escape of expanding gases under all but the most extreme conditions <sup>(13)</sup>. These conditions can be fulfilled if the difference between the time characteristic of the spacecraft cabin or space suit and that of an astronaut's respiratory passages is such that a transient pressure differential of a sufficient magnitude builds up between the lung and ambient atmospheric pressures. Since the volume of the lungs varies with respiration, it is apparent that the time characteristic of the lungs also varies with the phase of expiration. The trans-thoracic pressure differential for patent airways would therefore be greatest when decompression occurs at the time of full inspiration.

The time characteristic of "explosive" decompression required for injury or death is unknown for humans <sup>(15)</sup>. The results of animal studies, reviewed by Luft <sup>(13)</sup>, indicate that a cabin V/A ratio of about 1.2 ( $\text{m}^3/\text{m}^2$ ), or a time characteristic of about 3 milliseconds, is associated with a 50 percent mortality. If such data can be reasonably extrapolated to man, only the apparently uncomplicated exposures of Sweeney <sup>(18)</sup>, who had the cabin V/A ratio about 1 ( $\text{m}^3/\text{m}^2$ ), have been within the expected lethal range. It has been noted, however, that even if these human decompressions occurred with the respiratory passages closed and the lungs at mid-respiratory volume, the change in ambient atmospheric pressure would have been insufficient, despite the low V/A ratio, for a critical overpressure of about 80 mm Hg to be produced in the lung <sup>(13)</sup>. Finally the point should be brought out that even though the rate of gas escape from the spacecraft cabin or space suit and from the lungs depends mainly on the molecular weight of the gas under consideration. The molecular weights of the various gases which are being considered for use as spacecraft cabin atmospheres are probably not of great significance in influencing the magnitude of the "explosive" decompression hazard.

In his discussion of lung injuries caused by "explosive" decompression with the respiratory passages patent, Luft <sup>(13)</sup> described three phases

of lung decompression. The first phase is under essentially isometric conditions, with no change in volume; it is due to the inertia in the system. This phase is probably associated with the highest transthoracic pressures. In the second phase, the transthoracic pressure is attenuated due to the expansion of the chest and the escape of gas through the airways. The third phase is again isometric. The chest is normally expanded until the overpressure is dissipated by the escape of gas through the trachea. Disruption of pulmonary tissues probably occurs to the greatest degree when these tissues reach their limits of tensile strength during the third phase. However, structural damage might also occur during the first and second phases. In these phases, the differences in acceleration of intrathoracic tissues under the impulsive pressure loading could result in disruptive lesions similar to those encountered in meteoroid blast (Chapter 12). Luft pointed to convincing experimental evidence that overdextension of the lungs and not the pressure pulse of the first and second phases per se is the mechanism primarily responsible for lung disruption. Animals given pneumothoraces have survived "explosive" decompressions which would have been absolutely fatal otherwise. This suggests but does not prove that distension is the critical factor <sup>(11)</sup>. The fact that surrounding an animal's trunk with an inelastic fabric or plaster cast markedly increases tolerance to "explosive" decompression further substantiates this view <sup>(4, 5, 14)</sup>.

Although highly unlikely, it is possible that an "explosive" decompression might occur when an astronaut's respiratory passages are closed, such as during swallowing and breath holding. Lung injuries occurring under these circumstances will be caused by the same mechanisms as those above. However, injuries due to over distension of the lung will always be more serious than those due to the pressure pulse of the first and second phases of lung decompression <sup>(13)</sup>. The pressure gradient ( $\Delta P_L$ ) across the lungs and passively distended chest wall in this situation can be estimated from the following relationship derived by Luft <sup>(13)</sup>.

$$\Delta P_L = \left[ \frac{V_i}{V_{\max}} (P_i - 47) \right] + 47 - P_f$$

$V_i$  is defined as the lung volume prior to decompression,  $V_{\max}$  as the maximum intact volume of the lungs,  $P_i$  as the initial ambient atmospheric pressure, and  $P_f$  as the final ambient atmospheric pressure which, in the space situation, would be zero. It is apparent from this equation that when the initial and final pressures of decompression are given, the volume of gas trapped in the lungs relative to their total capacity is the factor which determines the transpulmonic pressure gradient which could cause overdistension and disruption of lung tissues.

From the above equation, the pressure gradient which might exist across an astronaut's lungs and passively distended chest wall if an "explosive" decompression to a vacuum occurs while his respiratory passages are closed was calculated both for different ambient atmospheric pressures which are currently used in the spacecraft (7 psia and 5 psia) and space suit (3.7 psia), and three different lung volumes prior to decompression: full inspiration ( $V_i/V_{\max} = 1.0$ ), the normal end expiratory position ( $V_i/V_{\max} = 0.55$ ), and full expiration ( $V_i/V_{\max} = 0.25$ ). This data is presented in Table 3.1.

$\frac{V_i}{V_{\max}}$	$\Delta P_L$ at $P_i = 7.0$ psia (362 mm Hg)	$\Delta P_L$ at $P_i = 5.0$ psia ( 259 mm Hg)	$\Delta P_L$ at $P_i = 3.7$ psia (191 mm Hg)
1.0	362 mm Hg	259 mm Hg	191 mm Hg
0.55	220 mm Hg	164 mm Hg	121 mm Hg
0.25	126 mm Hg	100 mm Hg	83 mm Hg

Table 3.1 Pressure gradients ( $\Delta P_L$ ) which might exist across an astronaut's lungs and passively distended chest wall if an "explosive" decompression in space occurs while his respiratory passages are closed. They are calculated for different ambient atmospheric pressures. ( $P_i$ ) and lung volumes ( $V_i$ ) prior to decompression to a vacuum ( $P_f = 0$ ).

It is most interesting to note that all such pressure gradients under these conditions are over the previously stated critical level of about 80 mm Hg. Therefore an "explosive" decompression in space while an astronaut's respiratory passages are closed is considered a very great hazard from the standpoint of serious lung injury from overdistension.

The pathophysiologic effects of the pressure pulse and the lung overdistention which occur during an "explosive" decompression have been described by Hitchcock <sup>(9)</sup>, Karstens <sup>(10)</sup>, and others <sup>(2, 7, 13, 19)</sup>. Since these effects are similar to those produced by blast <sup>(3)</sup>, discussion of this area is reserved for Chapter 12.

"Explosive" decompression does not appear to have a serious pathophysiologic effect on the gastrointestinal tract. The gastrointestinal tract of experimental animals decompressed from 523 mm Hg to 87 mm Hg in 15 milliseconds showed no gross pathology <sup>(6)</sup>. It has been difficult to produce actual disruption of the gastrointestinal tract in animal experiments, even with the most severe decompressions <sup>(4, 16, 19)</sup>. In humans, abdominal gas pains caused by "explosive" decompression has usually been no more severe than that resulting from slower decompressions through the same pressure range <sup>(2)</sup>. As pointed out in Chapter 12, severe gastrointestinal dilatation might itself elicit a severe bradycardia. An expanded stomach might displace the diaphragm upwards and so possibly embarrass respiration <sup>(2)</sup>. A temporary gastrointestinal ileus might conceivably occur secondary to severe dilatation.

Expanding air in the middle ears should escape without producing injury, even during the most severe "explosive" decompressions. This is also true for the escape of air from the sinus cavities, provided that the sinus passages are unobstructed <sup>(2)</sup>.

### Clinical Manifestations

Since the pathophysiologic effects of "explosive" decompression on the lung are similar to those produced by blast, it can be assumed that

the clinical manifestations associated with lung involvement would be the same in both situations. These manifestations are described in Chapter 12.

As mentioned above, injuries from the rapid expansion of gas in the gastrointestinal tract and middle ear and sinus cavities are not an expected result of "explosive" decompression. Gastrointestinal distension might be associated with severe pain. Through a vagal reflex elicited by the distension, faintness or syncope might occur. Gastric distension might displace the diaphragm upwards, and so possibly embarrass respiration during the decompression period. A period of gastrointestinal ileus might conceivably follow severe distension. Expanding gases in the gastrointestinal tract might cause projectile vomiting and defecation.

### Diagnosis

The diagnosis of internally inflicted injuries of explosive decompression should in most cases be obvious from an astronaut's history and physical examination. Reference is made to the diagnosis of blast injuries to the lung in Chapter 12.

### Treatment

The treatment of the consequences of lung injury due to "explosive" decompression would be the same as those outlined for blast in Chapter 12.

Although injuries from the expansion of gas in the gastrointestinal tract are not anticipated, it should be mentioned that the oral intake of foods and fluids should be restricted until there is reasonable assurance that gastrointestinal distension has not produced an ileus. If ileus occurs, especially if it is accompanied by vomiting, nasogastric suction might be required.

### Externally Inflicted Injuries

From past experience, the most serious consequences resulting from the accidental "explosive" decompression of pressurized aircraft have been the few unfortunate incidents in which an individual located

in the direct vicinity of the opening has been physically blown out of the cabin with the blast of escaping air or has been severely injured by striking or by being struck by objects in the cabin <sup>(2)</sup>. The rush of air through communicating channels or narrow passageways is often sufficient to propel an object or person within these areas with projectile-like velocities. Thus it appears that injuries might be inflicted during an "explosive" decompression, especially if an astronaut is unrestrained and is either close to the decompression orifice or in a narrow passageway between parts of the spacecraft cabin, or if items of equipment or other materials in the spacecraft cabin become detached or fragmented at the moment of decompression. This missile hazard will be particularly great if the cause of the "explosive" decompression is a meteoroid penetration (Chapter 12). The role of spacecraft cabin volume in determining the magnitude of this hazard must be kept in mind, for the greater this volume, the greater the potential momentum of an astronaut's body and disrupted structures produced by decompression.

The principles of treatment of various externally inflicted injuries which could result from an "explosive" decompression are discussed in Chapter 14.



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## CHAPTER 4

### DECOMPRESSION SICKNESS

Past experience has indicated that astronauts may be exposed to a risk of decompression sickness during extravehicular operations which require decompression from an atmosphere containing an inert gas. Such a risk will also be present following an emergency or accidental decompression of an inert gas atmosphere to an ambient pressure at which death does not immediately result from acute hypoxia (Chapter 1) or the combined effects of acute hypoxia and ebullism (Chapter 2).

As will be pointed out in this chapter, analysis of the risk of decompression sickness suggests that the potential incidence of minor manifestations of decompression sickness is quite low, and of major manifestations extremely low. However, until ground simulator and space operational experience confirm this optimistic attitude, it remains advisable to consider and prepare for the treatment of decompression sickness, especially for missions during which there will be much extravehicular activity.

A detailed discussion of decompression sickness here would be redundant in the light of many excellent reviews which have covered all known aspects of this syndrome, particularly as it occurs following ascent to altitude (20, 44, 64, 65, 79, 81, 88, 89). This brief presentation summarizes only those aspects of decompression sickness considered pertinent to the occurrence and treatment of it in space. Further detail in this area can be sought in the key literature cited.

#### Pathophysiology

The pathophysiology of decompression sickness has received detailed consideration by Adler (1, 2), Catchpole and Gersh (18), Clamann (20), Harvey (46), Haymaker and Johnston (47), Kern (59), Luft (64), Rait (79), Wittmer (89), and many others (3, 7, 14, 19, 22, 23, 44, 77, 80, 81).

The following discussion is mainly concerned with the basic mechanisms involved in the production of this syndrome and the risk of its occurrence

relative to the use of various inert gases which might be considered for use in spacecraft cabin atmospheres. More specific pathophysiologic mechanisms will be considered in the subsequent discussion of the clinical manifestations of decompression sickness.

Many theories have been advanced to explain the various manifestations of decompression sickness. Most investigators believe that this syndrome results from the pressure and volume effects of bubbles which appear in the blood and tissues of the body when the sum of the partial pressures of gases dissolved in the body fluids becomes sufficiently greater than that of the ambient atmosphere.

The literature pertinent to the formation and growth of bubbles formed in decompression sickness has been summarized by Roth<sup>(81)</sup> and others<sup>(3, 20, 33, 59, 64)</sup>. It is thought that bubbles most likely originate as water vapor cavities in areas where large local decreases in hydrostatic pressure can occur<sup>(81)</sup>. Such areas include moving joints, the insertions of contracting muscles, and vortices of turbulent zones of blood flow. It has also been suggested that a bubble might originate from a stable bubble nucleus formed in tiny hydrophobic niches in tissue structures<sup>(20, 21)</sup>. The occurrence of pressure pulses and the propagation of sound waves have even been postulated as mechanisms in initiating bubble formation<sup>(20)</sup>.

Whatever focal event might be responsible for initiating bubble formation, an essential prerequisite must apparently be fulfilled before a bubble can persist and grow to a size at which it can exert pathophysiologic effects. The sum of the partial pressures of gases dissolved in the fluid surrounding a bubble must be sufficiently greater than the absolute pressure (hydrostatic pressure plus ambient atmospheric pressure) being exerted on the fluid. This pressure difference then favors bubble growth from diffusion of gases into the bubble. In this respect, the nitrogen (or other inert gas) in the atmosphere which is breathed prior to decompression becomes the major contributor to bubble growth, due to its high partial pressure as compared to other dissolved gases at the sites where bubbles tend to form and grow. In the absence of gaseous super-

saturation of the surrounding fluid, a bubble will eventually collapse, the dissolution of gases and water vapor in it being driven mainly by the surface tension of its wall.

The initial rate of growth of a decompression bubble is proportional to the total amounts of gases available at the liquid-vapor interface. Because carbon dioxide has a higher permeation coefficient than other gases, it is the main early constituent of bubbles formed at altitude. This appears to account for the greater propensity for decompression sickness when exercising at altitude, and possibly for the fact that most decompression symptoms which occur at altitude rapidly disappear following a relatively slight increase in the ambient atmospheric pressure (7, 11, 46, 51, 64, 81). As a bubble continues to grow, both the amounts of gases in the fluid surrounding the bubble and the diffusion constants of these gases will determine the rate of bubble growth. In time, the relative proportions of gases in a bubble will become proportional to the partial pressures of these gases in the surrounding fluid medium (81).

The non-supersaturated blood which circulates through a tissue or past an intravascular site where a bubble is formed affects the growth rate as well as the peak size and rate of decay of the bubble. After decompression, the systemic venous blood, for all practical purposes, loses all of its supersaturated gas in passing through the lungs (15). Accordingly, as soon as a bubble is formed it begins to compete for gases with surrounding supersaturated tissues which are in turn being perfused, and so desaturated, by non-supersaturated blood. The degree of support given to bubble growth by a tissue will therefore be directly proportional to the rate of gas desaturation of the tissue. This rate which will depend on the relative solubility of nitrogen or other inert gas in the tissue as compared to blood, on the rate of blood perfusion of the tissue and, apparently to a very minor degree, on the diffusibility of the gas through the tissue (56, 81). Taking solubility and perfusion factors into account, it is obvious why poorly perfused adipose or fatty tissues, in which nitrogen has a high solubility, support bubble growth so well. A favorable situation for bubbles also exists in poorly perfused

tissues such as fibrous tissue, cartilage and bone.

The ultimate size which an expanding bubble can attain is determined by the distensibility of the medium surrounding the bubble. Loose tissues favor the growth of large bubbles, which are usually asymptomatic due to the low deformation pressures associated with their growth. On the other hand, tight tissues such as tendons and joint capsules limit growth of bubbles. Such bubbles reach maximum sizes rather quickly and are associated with high tissue deformation pressures which, by triggering of pain responses and reflex vasospasm, disrupting tissues, and compromising tissue blood flow, are apparently responsible for many of the manifestations of decompression sickness.

Roth <sup>(81)</sup> has assessed the role which various inert gases might play in determining the rate of pressure or volume rise of a bubble and, therefore, in determining the risks of decompression sickness. Such an evaluation is quite pertinent to the selection of suitable spacecraft atmospheres. It also assists in the determination of appropriate measures which an astronaut might take in an operational situation, prior to and while decompressing from an atmosphere containing an inert gas, in order to prevent the occurrence of decompression sickness. Helium, neon and nitrogen appear to be the most suitable gases to consider for use in spacecraft cabin atmospheres. In the light of both his theoretical predictions and available empirical data, Roth concluded in essence that:

- theory and empirical data indicate that the potential incidence of the minor manifestations of decompression sickness after decompression from an atmosphere containing helium probably does not differ from that after decompression from an atmosphere containing nitrogen, assuming that the inert gas and oxygen compositions are similar in both atmospheres. Neon might be somewhat more favorable than either helium or nitrogen in reducing this incidence.

- theory indicates more striking differences between the various inert gases as far as the potential incidence of the major manifestations of decompression sickness is concerned. Although the potential incidence of "chokes" should be about equal for nitrogen and helium, the potential incidence of cardiovascular

and neurologic manifestations should be much less for helium than for nitrogen. Roth noted, however, that evidence from diving experiments indicates a less distinct difference between these gases. On theoretical grounds, neon should yield the lowest incidence of these manifestations of decompression sickness.

-empirical data in this area is greatly needed.

### Clinical Manifestations

The clinical manifestations of decompression sickness experienced by an astronaut would be similar to those of decompression sickness at altitude described by Adler <sup>(1, 2)</sup>, Clamann <sup>(20)</sup>, Ferris and Engel <sup>(36)</sup>, Kern <sup>(59)</sup>, Luft <sup>(64)</sup>, Gribble <sup>(44)</sup>, Roth <sup>(81)</sup>, and McIver <sup>(70)</sup>. Reference is made to many clinical reports of cases of decompression sickness at altitude (9, 10, 17, 21, 26, 31, 38, 54, 65, 68, 71, 82, 87). The pathologic findings in fatal cases have also been well documented <sup>(2, 10, 18, 26, 47, 65, 69, 76)</sup>. Reference is also made to differences in the clinical manifestations of decompression sickness between aviators and divers <sup>(44, 47, 59)</sup>.

Decompression sickness occurs in aviators after an ascent from ground level conditions of about 760 mm Hg (14.7 psia) to ambient atmospheric pressures of apparently always less than about 380 mm Hg (7.3 psia, 18,000 ft.), and usually less than 320 mm Hg (6.2 psia, 22,000 ft.) <sup>(39, 59, 81)</sup>. It should be noted that the latent period, rate and peak frequency of clinical manifestations of decompression sickness appearing after ascent are primarily functions of altitude and physical activity. Theoretical predictions of Nims <sup>(75)</sup> were substantiated by Anthony and co-workers <sup>(4)</sup> who observed that even under the most predisposing circumstances, signs and symptoms of decompression sickness may not appear for at least 5 to 10 minutes after a decompression event. Their rate of onset was found to increase to a peak in about 20 to 40 minutes, and then to decline practically to zero 2 hours after decompression. It is interesting to note that the clinical manifestations of decompression sickness have been found to appear sooner when helium as opposed

to nitrogen is the diluent gas in the pre-decompression atmosphere (6). It should be noted, however, that this observation was made in short term experiments so that some nitrogen might have remained in tissues from the original air exposure to contribute to the production of "helium 'bends' ".

The marked influence which physical activity has on the rate of appearance of clinical manifestations of decompression sickness deserves emphasis here, especially in the light of the fact that extravehicular operations in space will be associated with strenuous physical activity. This relationship was studied intensively by Henry (51) who published data presented graphically in Figure 4.1.

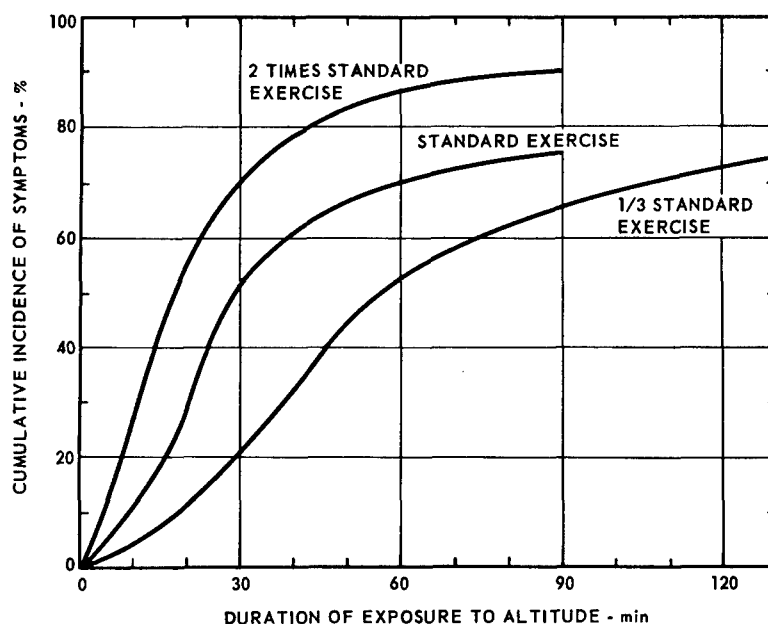


Figure 4.1 Effect of physical activity on appearance of clinical manifestations of decompression sickness at 38,000 feet. Standard exercise was 10 step-ups onto a 9 inch stool in 30 seconds, repeated every 5 minutes.

(After Henry (51), redrawn for Bioastronautics Data Book (74))

The clinical manifestations of decompression sickness in aviators fall into four categories - "bends", "chokes", skin manifestations, and



neurocirculatory manifestations.

### "Bends"

"Bends" is the term used for most common clinical manifestations of decompression sickness. It is characterized by musculoskeletal discomfort which is usually described as a deep, poorly localized, waxing and waning, dull, gnawing pain which ranges in severity from mild discomfort to excruciating agony. "Bends" pain usually begins in the peri-articular tissues, and then radiates distally along the bone shaft. Reflex weakness of the involved limb commonly occurs. "Bends" can be somewhat relieved by relaxing or applying pressure over the painful area. It may even gradually subside in intensity if the afflicted individual is able to "sit it out". However, the increased risk of other more serious manifestations of decompression sickness occurring if a decompression exposure is prolonged must be kept in mind.

"Bends" are prone to occur in the joints that are involved in motion, especially the knees, ankles, shoulders, wrists, and elbows. Instances of "bends" pain in the sternum, ribs, cranium, and vertebrae have also been reported (1, 2). The popular notion that "bends" is prone to occur at sites of previous injury has not been substantiated (20, 42). Notably, it is rare for this symptom to appear after 90 minutes exposure to altitude. Practical inflight experience has demonstrated that exposure to cold makes one more likely to develop decompression sickness, especially "bends".

X-ray findings of bubbles and the clinical pictures presented by individuals suffering from "bends" have in general correlated poorly (16, 36). Bubbles with and without associated symptoms have been seen on x-ray in synovial spaces of joints, in bursae, and in vaginal sheaths of tendons (12, 36, 84). They have apparently also been seen in fascial planes and connective tissue spaces in muscles, and in tissue spaces around blood vessels (55, 83). Crepitation has also been felt along tendon sheaths in which gas bubbles were visualized by x-ray (36). X-ray studies in animals have indicated that some of the thin radiolucent lines and more diffuse areas which have been attributed to extravascular bubbles

may actually be long, cylindrically-shaped intravascular bubbles (18). The presence of bubbles in veins leading from exercising muscles also suggests that intravascular bubbles at muscular insertions could be a cause of "bends" (16, 18, 46).

It is a well known fact that on descent, "bends" almost invariably disappears completely. Of interest is the recent observation that "nitrogen 'bends' " were relieved at somewhat lower pressures than "helium 'bends' " (6). Immediate reascent causes crepitus and x-ray findings to return, thus indicating that the bubbles are compressed but their contained gases are not completely redissolved until some time after descent (30, 36). As the time period between exposures to decompression events lengthens, the time of onset and the progression of "bends" pain are slowed (83). Re-exposure after 24 hours "on the ground" is apparently not accompanied by an increased "bends" susceptibility over that seen regularly (59). Twinges of pain may occasionally be experienced in the affected part up to 5 days post-exposure. In very rare instances, signs and symptoms of mild inflammation may develop in the affected part and reach a peak intensity 12 to 36 hours post-exposure.

The marked influence which physical activity has on the occurrence of "bends" deserves further comment. It is noted that straining exercise is not only a factor in the location of "bends", but also a very important factor in influencing the incidence of "bends" and the speed it develops once altitude is reached (36, 43). By the same token, strenuous physical activity has been shown to lower the altitude threshold for this manifestation by several thousand feet (20, 25, 37). For example, such activity was found to increase the total number of "bends" incidents and shift the ratio of light to severe "bends" from 38,000 feet (155 mm Hg or 3.0 psia) to 28,000 feet (247 mm Hg or 4.8 psia) (20). Increasing the frequency of exercise may decrease this threshold still further. Although the mechanism whereby muscular activity intensified the incidence and severity of these manifestations is still controversial, as mentioned previously, elevated local partial pressures of carbon dioxide and large mechanically induced negative pressures associated with

muscular action appear to be the major contributors to this intensification.

### "Chokes"

"Chokes" is the next most common clinical manifestation of decompression sickness. It usually occurs after a longer exposure to altitude than that required for "bends". "Chokes" is an alarming peculiar form of substernal distress, characterized by chest pain, cough and respiratory distress, all of which are aggravated by deep inspiration or coughing. The appearance of this symptom complex is usually heralded by an inspiratory, substernal burning pain which is relieved by deep inspiration. This pain gradually increases in severity and is experienced during all phases of respiration. Paroxysms of non-productive coughing commence and become more and more frequent. Breathing becomes difficult and the affected individual experiences a sense of suffocation and apprehension. In late stages, cyanosis, syncope and "shock" can occur. The clinical manifestations of "chokes" are ameliorated by descent, but can persist for several hours depending on the period of time they are suffered at altitude. During this period, deep breathing can cause a recrudescence of symptoms.

Strangely, a fiery red mucosal lining in the pharynx and larynx is often seen in cases of "chokes". This sign can persist for many hours after descent. Auscultation, x-rays and electrocardiograms have never shown any very specific abnormalities in "chokes". Right heart dilatation has been seen in x-rays taken during "chokes" (16). Rales and x-ray findings of pulmonary congestion have been observed for a few hours after descent (59).

"Chokes" is currently thought to be due to a reflex phenomenon arising from irritation of the pulmonary tissues by gas emboli which obstruct blood flow through pulmonary arterioles and capillaries (81). Animal studies have supported this view (48, 63, 70, 72). In such studies, marked bubble formation on the venous side of the circulation following a decompression event was found to be associated with a rapid shallow respiration and pulmonary hypertension. Although quite variable, the clinical syndrome resulting from the intravenous injection of air in

humans often resembles "chokes" (81). As will be discussed below, the possibility that fat emboli from disrupted adipose tissue can lodge in the pulmonary vessels, and so play a role in producing "chokes", remains controversial.

### Skin Manifestations

The skin manifestations of decompression sickness are mild, usually occurring only after a relatively prolonged exposure to a decompression event (36). They may occur in conjunction with or presage more serious manifestations of decompression sickness. It is notable that about 10 percent of those cases progressing to circulatory collapse present previous skin manifestations (81). Four types of skin manifestations have been described.

1. A subjective cold sensation can be experienced during decompression. This sensation may or may not be due to decompression per se.
2. Tiny intracutaneous gas blebs can appear and produce an intense itching sensation which is usually referred to as "creeps". Prickling and burning sensations are also commonly associated with these blebs, which might in fact be gases trapped in the glands of the skin (81).
3. Subcutaneous emphysema rarely occurs. It is usually found on the forearms and thighs, where it can produce moderate pain and tenderness. Crepitus can be felt and gas can be seen on x-ray.
4. Actual skin lesions can occur. These lesions appear most frequently in individuals who are for some reason susceptible to "chokes". They are usually found on the chest, shoulders, and abdomen. A lesion first develops in a small skin area, then spreads out irregularly in all directions. In early stages it has a pale, mottled, cyanotic appearance. Later its center becomes erythematous and warm. Mild to moderate pain may occur at this stage; crepitus has not been found (81). During descent, this skin lesion becomes diffusely red and hot, and usually disappears about 3 to 5 minutes after descent. Four to 6 hours later, the lesion area again becomes tender. This

delayed response is maximal at 24 to 36 hours after descent, and can be associated with subcutaneous edema which may persist for several days.

It is probable that gas emboli in skin blood vessels is the cause of this clinical manifestation of decompression sickness. The mottled cyanotic appearance of the involved skin area is apparently due to the dilatation of superficial venules and capillaries adjacent to areas of severe vasoconstriction (81). This phenomenon can even result in petechial hemorrhages from damaged capillaries. Although subcutaneous fat is a source of these emboli, it has been suggested that emboli from this and other sources reach the cutaneous vessels at altitude by passing from the venous to the arterial side of the circulation through the large pulmonary arteriovenous shunts and in rare instances, through a patent foramen ovale (18). However, there is the possibility that gas emboli also form within the arterial system (81).

#### Neurocirculatory Manifestations

The cardiovascular and neurologic manifestations of decompression sickness have usually been described under this heading (1, 2, 10, 14, 36, 65, 68, 81). This is no doubt due to the fact that these manifestations often occur together and are the most serious, variable, poorly understood, rarely occurring manifestations of this syndrome.

Malette and co-workers (65) separated cases suffering from neurocirculatory manifestations of decompression sickness into two clinical categories. In one category, the signs and symptoms of disturbed cardiovascular function predominated. In the other, those of disturbed neurologic function predominated. At opposite ends of the scale were cases with only cardiovascular or with only neurologic manifestations. Between these extremes were various mixtures, with the clinical findings of the one or other category predominating. It is of interest to note that when these cases were arranged in this manner, no fatalities occurred in the group whose manifestations were only neurological (26, 65). On the other hand, when cardiovascular disturbances were part of the clinical picture, a very significant mortality rate existed.

A fall in systemic arterial blood pressure, often accompanied by a

marked bradycardia can occur at altitude. This reaction can be accompanied by the usual symptoms of arterial hypotension, such as pallor, perspiration, faintness and loss of consciousness. Hypotensive episodes reportedly occur in about 10 percent of severe "bends" and 25 percent of "chokes" cases, and can also be associated with decompression effects which are not usually classified as decompression sickness, such as gastrointestinal distension, aerosinusitis and aerotitis media (1, 20). It should be noted that certain signs and symptoms similar to those due to, but not associated with hypotension, can occur at altitude (36, 59). Hyperventilation is associated with manifestations such as paresthesias, lightheadedness, reduction in consciousness and tetany. Manifestations of acute hypoxia have been outlined in Chapter 1. Lightheadedness can be associated with the paroxysms of coughing and cyanosis due to "chokes". In such a case, actual loss of consciousness is rare.

Hypotensive episodes at altitude are usually relieved immediately by descent or within 30 minutes thereafter (59, 81). Quite rarely, however, hypotension persists to a varying degree. In this case circulatory collapse, or the so-called delayed "shock" syndrome, frequently occurs in less than one hour to several hours after descent. Notably, this syndrome is most likely to appear in individuals who have experienced major manifestations of decompression sickness at altitude, especially severe "chokes". However it has arisen on rare occasions without any premonitory or minimal signs or symptoms of decompression sickness having occurred at altitude (81).

It appears that any one or more of a number of mechanisms might be the cause of hypotension at altitude. In all probability, the simple syncopal, or vasovagal reaction is the commonest mechanism. An explanation of the cause of syncope associated with "chokes" must take into account various factors, such as reflex bradycardia induced by the chest pain or by gas or other emboli in the pulmonary circulation, cardiac insufficiency due to extensive blockage of the pulmonary circulation by these emboli, and the peripheral vasodilatory effects of hypoxia and secondary hypercarbia which can occur with "chokes". Cases of

syncope at altitude have been associated with frank cardiac disturbances such as coronary occlusion, paroxysmal auricular fibrillation and bundle branch block <sup>(8)</sup>. A bubble or bubbles entering the coronary arterial system might well have been the cause of death in one of the cases of decompression sickness reported by Robie and co-workers <sup>(80)</sup>. Finally, it is conceivable that vasodepressor syncope might result from an autonomic imbalance caused by embolic damage of the central nervous system.

The delayed "shock" syndrome is characterized by a marked loss of plasma into the extravascular compartment, especially in the form of pulmonary edema and pleural effusion. It has been shown in recent animal experiments and assumed in the numerous human cases of the delayed "shock" syndrome cited above that death from hypovolemic "shock" can occur unless measures are taken immediately to supplement the diminishing blood volume <sup>(23, 24)</sup>. The basic mechanisms underlying this syndrome are, however, an enigma. The fact that it has been effectively treated by hyperbaric recompression supports the view that the shock is secondary to a scattering of air emboli throughout the body <sup>(10, 13, 21, 31, 32, 81)</sup>. As mentioned previously, bubbles formed in tissues at altitude might conceivably cross over from the venous to the arterial side of the circulation while an individual is at altitude. However, it is possible that this phenomenon would more likely occur during and after descent, when the bubbles have been made smaller. The probable routes of bubble passage are considered to be both well defined, anatomically normal shunts such as pulmonary arteriovenous anastomoses, bronchovenous shunts and large pleural capillaries, and pathologic shunts such as a patent foramen ovale <sup>(14, 18, 47, 65, 76, 89)</sup>. This cross-over concept becomes even more plausible when one takes into consideration the fact that high pulmonary arterial, and hence right heart pressures which can result from embolic blockage of the pulmonary circulation, would tend to drive bubbles through these shunts. It is also thought that bubbles can also be formed on the arterial side of the circulation <sup>(81)</sup>.

The question arises as to why "shock" characteristically appears

some time after descent. As mentioned above, decrease in bubble size by descent may favor bubble cross-over. It has also been suggested that as a bubble gets smaller, it is more apt to migrate distally beyond collateral circulation points, and so produce ischemia <sup>(81)</sup>. As well, one must remember that decompression bubbles can persist for many hours before they are absorbed completely <sup>(33, 46)</sup>. These bubbles would then exert their damaging effects on blood vessels for some time, so that the clinical onset of "shock" from loss of plasma sufficient to produce this manifestation would be justifiably delayed. Finally, it should be noted that the marked loss of intravascular fluid into the lungs and pleural "space" might be due to the fact that the lungs act as a filter for emboli, and hence would be more likely to suffer more embolic damage than would be expected in other tissues.

The reason for the increased capillary permeability in the delayed "shock" syndrome is as yet to be defined. It is probable that tissue hypoxia from vessel blockage and irritative vasospasm induced by bubbles renders capillaries hyperpermeable. Since heparin appears to confer some protection on animals undergoing decompression, it has been suggested that bubbles promote platelet clumping, agglutination of erythrocytes and formation of plasma flocculates which lead to vascular thromboses <sup>(5, 41, 61)</sup>. Blockage of vessels by thrombi could then enhance the damaging effect of bubbles. In contrast to this success with heparin, however, a similar series of experiments failed to demonstrate any protective action of another anticoagulant, bishydroxycoumarin <sup>(41)</sup>. One explanation for this difference in findings is the possibility that heparin exerts its major protective effect through its antiproteolytic activity, which would tend to diminish the vasodilatory and injurious effects of the breakdown products of hypoxic tissues on vessel walls <sup>(5)</sup>. Another explanation centers on the observation that partially depolymerized hyaluronic acid (PDHA) has also had a protective action in decompressed animals. Interestingly, both heparin and PDHA have lipemia-clearing activity <sup>(41)</sup>. The possible implications of this are discussed below. Finally, it has been thought possible that biologically-active substances such as bradykinin, histamine, and sero-



tonin might be triggered in tissues by bubble expansion or blockage of blood flow, and so participate to some extent in the production not only of the delayed "shock" syndrome but also of other manifestations of decompression sickness (27, 60).

A not infrequent finding in fatal cases of decompression sickness has been the presence of microscopic fat emboli in the small arterial vessels and capillaries throughout the body, especially in the lungs (47, 65, 76, 80). These emboli have also been demonstrated in animal decompression experiments (19, 22, 23). The source and role of these emboli in the etiology of the delayed "shock" syndrome remains unclear (81). Murray (73) has postulated that the high concentration of total circulating lipids associated with "shock", severe illness and trauma is due to the mobilization and subsequent aggregation of fat from body fat depots through increased activity of a hypothalamic "fat center". After finding more cholesterol in fat emboli than in depot fat in decompressed animals, LeQuire and co-workers (62) suggested that fat emboli of decompression sickness form primarily within the circulatory system as the result of physiochemical alterations induced by products of tissue damage and "shock", rather than by entering the circulatory system from fat depots disrupted by decompression bubbles. Further support for an intravascular aggregation of fat in decompression sickness has been given by the observations that heparin and PDHA, both of which have fat-clearing activity, confer significant protection on animals undergoing decompression (41).

In contrast to the views expressed above, Whiteley (86) could find no experimental evidence which would lend support for an intravascular aggregation of fat in decompression sickness. He postulated that fat enters the circulation at the site of tissue injury and that an injury itself can somehow modify the vascular bed, making it more sensitive to intravascular fat. Rait (79) has outlined a specific mechanism for the release of fat emboli from tissues into the circulation in decompression sickness. The presence of both fat emboli and a fatty liver in many of the fatal cases of decompression sickness studied suggested to him that a causal relationship existed between these findings. It appeared that a fatty liver

under decompression ideally fulfills the three requirements, stated by Harris <sup>(45)</sup>, for fat embolism to occur. Firstly, a fatty liver contains a free, fluid, readily mobilizable fat. Secondly, the liver is essentially indistensible, so that intrahepatic tissue pressures higher than the hepatic venous pressure can develop as bubbles form in fatty hepatic cells. Thirdly, the liver possesses patent veins with open ends which do not collapse (sinusoidal system). Rait also noted that the presence of bone marrow emboli and, in some cases, fat emboli in fatalities from decompression sickness might also be explained by applying this mechanism to the bone marrow. Finally, he supported his fatty liver concept by pointing out that dietary management directed at reducing the prevalence of fatty liver in the Royal Australian Air Force has apparently accounted for the low incidence of the delayed "shock" syndrome in this group.

Intravascular fat could produce hypoxic tissue damage by interfering with blood flow. It could also hydrolyse into free fatty acids which would damage capillary endothelium, and so render it hyper-permeable. It is thought that the means by which fat emboli cross over from the venous to the arterial side of the circulation would be the same as that described above for bubbles, and that the lungs would again bear the brunt of embolic damage due to their filtering action. Also of interest is the fact that the circulatory collapse due to traumatic fat embolism is also a delayed phenomenon, if death does not occur immediately due to acute right ventricular failure secondary to blockage of pulmonary blood flow. This delay has been attributed to the time required for sufficient fatty acids to be released and subsequently exert their damaging effects <sup>(78)</sup>.

Finally it should be pointed out that recent animal studies of Henn and Wünsche <sup>(49)</sup> might have shed some light on the roles of bubble and fat emboli in producing the delayed "shock" syndrome of decompression sickness. These investigators suggested that the time of ascent to altitude was critical in determining the type of emboli produced. Roth <sup>(81)</sup> has summarized the data from their experiments, which indicated that there might be both altitude and rate thresholds for the pro-

duction of fat emboli. A review of the literature on fatal cases of decompression sickness and two cases of their own in which fat emboli were found suggested that an ascent rate between 8 and 12 Km/min (26,400 to 37,000 ft/min) is the threshold for fat emboli in humans. Roth pointed out, however, that rates of 1000 to 1500 m/min (3000 to 4800 ft/min) have also been associated with fat emboli in humans (81). Further investigation of this phenomenon is indicated.

The neurologic manifestations of decompression sickness are usually of a highly diversified but focal nature (59). As pointed out above, they are frequently associated with other manifestations of decompression sickness. Those that develop at altitude are usually transitory, lasting minutes to a few hours after descent (20). They can also appear at any time up to 12 hours after descent from altitude (81). The most common neurologic manifestation is a homonomous, scintillating scotoma with sparing of central vision (87). Other possible signs and symptoms include various hemipareses, monopareses, focal or generalized convulsions, aphasias, sensory disturbances and sensorial clouding (1, 20, 59, 81). It is noted that such important signs as impairment of judgment and inability to assess the true nature of the situation can be pronounced (71). Such manifestations can vary considerably before a stabilized clinical picture is established.

The disappearance of neurologic manifestations of decompression sickness is frequently followed by an intense throbbing headache on the side which is contralateral to the neurologic lesion. This headache has been occasionally experienced, however, without an antecedent neurologic event (59). This headache is often associated with nausea, vomiting, prostration, photophobia, and increased pain on head movement. It usually lasts from one to 12 hours in duration.

Those neurologic manifestations with a delayed onset can take up to several weeks to disappear (20). Reported cases of permanent neurologic sequelae of decompression sickness in aviators have been exceptionally rare, in contrast to such cases in divers (9, 20, 44, 59).

The electroencephalogram of individuals suffering from neurologic

manifestations of decompression sickness usually shows irregular slow waves at foci corresponding to neurologic findings <sup>(81)</sup>. It shows no abnormalities in those suffering from the headache described above, however.

It should be noted that the neurologic manifestations of decompression sickness do have to be distinguished from other neurologic signs and symptoms which can also occur at altitude. A convulsion can result from cerebral hypoxia accompanying a hypotensive episode or from a hypoxic exposure <sup>(59)</sup>. Weakness of an extremity simulating a neurologic lesion can be seen with "bends". As well, neurologic signs and symptoms can be caused by hypocapnia associated with hyperventilation.

The neurologic manifestations of decompression sickness are generally thought to be caused by focal hypoxia of brain tissue, not only from a blockage of blood flow, but also from local vasospasm induced by vascular irritation by bubbles <sup>(1, 90)</sup>. There is also the possibility that such manifestations might be caused by bubbles forming in cerebral veins and tissues. Interestingly, the incidence of spontaneous migraine is apparently higher in those individuals who develop a scotoma and headache associated with decompression sickness at altitude; similar electroencephalographic findings have been recorded in both instances <sup>(38, 59, 68)</sup>. This would lead one to speculate that bubbles might be preferentially generated at a turbulent site in the cerebral arterial tree, and hence tend to lodge in the same area of the occipital cortex after each altitude exposure <sup>(81)</sup>. Otherwise, the various mechanisms postulated for delayed "shock" syndrome have also been applied to the neurologic manifestations of decompression sickness. It is interesting to speculate that fat emboli might be the cause of at least some delayed neurologic manifestations, especially those which require a prolonged period for recovery or leave permanent sequelae.

#### Diagnosis

For the purpose of diagnosis, the requirement for thorough familiarity with the numerous recorded cases <sup>(2, 9, 10, 17, 18, 21, 26, 31, 38, 54,</sup>

65, 68, 71, 82, 85, 87) as well as the general aspects of decompression sickness cannot be overstressed. Any otherwise unexplainable sign or symptom which appears while an astronaut is in a decompression situation should be presumed to be a manifestation of decompression sickness. The strongest evidence supporting the occurrence of this syndrome would obviously be the relief or alteration of signs and symptoms by recompression.

Most important from a diagnostic standpoint are a detailed history, thorough physical examination and subsequent close observation of an astronaut who has experienced manifestations of decompression sickness such as severe "bends", "chokes", syncope and neurologic signs and symptoms while in a decompression situation, especially if signs and symptoms persist for some time after recompression. As noted above, the delayed "shock" syndrome is frequently preceded by such manifestations. Cardiovascular function should be monitored by repeatedly recording both pulse rate and systemic arterial blood pressure. Frequent recording of the hematocrit, if possible in space, should be undertaken to diagnose plasma loss. An electrocardiogram might be indicated if embolic myocardial damage is suspected. As mentioned previously, focal neurologic involvement in decompression sickness is usually associated with typical electroencephalographic abnormalities over the involved brain area.

### Prevention

If an astronaut could be exposed for operational reasons or in an emergency to an ambient pressure at which decompression sickness can occur, the risk of this condition developing can be lessened by several means. Most apropos to the space situation is the selection of a suitable pressure and inert gas composition of the atmosphere from which and to which an astronaut can have a safe, rapid decompression. Another measure which would be feasible to undertake in space is preoxygenation.

The use of pure oxygen atmospheres in space would be the ideal preventive measure for decompression sickness. However, as Roth (81) pointed out in his recent assessment of atmospheres which have been

suggested for use in space, risks of fire and oxygen toxicity in particular mitigate against the use of pure oxygen as a spacecraft cabin atmosphere. On theoretical and empirical grounds, he predicted the risks of decompression sickness which would be present if an astronaut, who had been equilibrated with various 50 percent inert gas-oxygen mixtures in a spacecraft cabin at 7.0 psia (354 mm Hg) atmospheric pressure, is decompressed. He noted that rapid decompression from such an atmosphere, containing nitrogen as its inert gas, to a space suit atmosphere containing 100 percent oxygen at 3.5 psia (179 mm Hg) would be associated with a marked reduction in both the frequency and severity of "bends", as compared to a similar decompression from air at 14.7 psia (760 mm Hg). He predicted that the incidence of "bends" in a physically fit astronaut in equilibrium with such an atmosphere should be less than 7 percent if moderate exercise is performed, as was essentially the finding in human experiments (28, 29), and much less than one percent during piloting operations or while an astronaut is at rest. These values were about three times those predicted for decompression to 100 percent oxygen at 5.0 psia (258 mm Hg). Considering the risk of decompression sickness associated with other inert gases, Roth predicted that helium might be associated with a greater "bends" frequency than nitrogen. This appears to have been substantiated by recent experiments, which also showed that "helium 'bends'" appeared sooner than "nitrogen 'bends'" (6, 58). Finally, Roth noted that there is theoretical evidence supporting neon as producing a much lower incidence of neurocirculatory manifestations, "chokes", and even "bends" than either nitrogen or helium. Others have arrived at similar conclusions using slightly different physical models (6).

Preoxygenation, or the continuous breathing of 100 percent oxygen for a period of time before decompression can be highly effective in preventing decompression sickness (6, 20, 28, 29, 58, 66, 67, 81). Since this procedure must allow tissues which desaturate slowly to reach a "safe" level of dissolved nitrogen or other inert gas, the duration of preoxygenation is the major factor in determining its success. Even

if an astronaut has a short period of preoxygenation before decompression, the risk of suffering from decompression sickness will diminish. As well, the duration of decompression before signs and symptoms of decompression sickness appear will decrease (52, 57, 66, 67). It should be noted that this latent period can be shortened somewhat if preoxygenation is accomplished while an individual is being decompressed, presumably due to the formation of silent bubbles at pre-"bends" altitudes (50, 58, 81). Increase in age, physical conditioning, and physical activity during preoxygenation decrease the time required to accomplish an adequate preoxygenation (20, 64, 66, 81).

Preoxygenation rules for astronauts have also been suggested by Roth (81) in his detailed assessment of this area. He recommended a minimum of two or possibly three hours preoxygenation time for astronauts who have been breathing air at 14.7 psia (760 mm Hg) to equilibrate to the level of total body nitrogen in a 50 percent nitrogen-oxygen mixture in a spacecraft cabin at 7.0 psia (364 mm Hg) atmospheric pressure. He predicted that without preoxygenation, it would take an astronaut about 8 hours to equilibrate with this atmosphere. Whether preoxygenation should be carried out prior to decompressions from a 50 percent inert gas-oxygen mixture in a spacecraft cabin at 7.0 psia (364 mm Hg) atmospheric pressure to 100 percent oxygen at 3.5 psia (179 mm Hg) space suit atmosphere remains debatable, however, especially in the light of the low risk and mild clinical manifestations anticipated from such decompressions. When carried out for one-half hour in recent simulations of these space atmosphere exposures, this measure was quite effective in preventing "nitrogen 'bends' " but apparently was not effective in preventing "helium 'bends' ", although the symptoms of "helium 'bends' " had more of a tendency to disappear spontaneously when decompression exposures were continued (6). It should be pointed out that these were short-term experiments, so that some nitrogen might have remained in tissues from the original air exposure, to contribute to the production of "helium 'bends' " following

decompression from the 50 percent helium-oxygen atmosphere at 7.0 psia.

Finally, it should be pointed out that an astronaut who experiences any manifestation of decompression sickness should be restricted, if possible, from being decompressed for at least 24 hours.

### Treatment

Once a presumptive diagnosis of decompression sickness has been made, an afflicted astronaut should be recompressed as soon as possible to at least the atmospheric pressure with which he was equilibrated before decompression. "Bends" will in most instances completely disappear on recompression. If not, local pressure and massage over the involved joint areas may bring some relief. "Chokes" symptoms should be ameliorated, but might persist or recrudesce on deep breathing up to several hours after recompression. During this period, a suitable analgesic might be required for the relief of such symptoms. It does not appear to have been established whether the breathing of 100 percent oxygen is of greater value than the breathing of other gas mixtures in the relief of "chokes" symptoms.

The major aspects of the treatment of decompression sickness center on its cardiovascular and neurologic manifestations. The fact that little is known about the specific pathophysiologic mechanisms involved in producing these manifestations should be kept in mind. Accordingly, therapeutic measures suggested here may be inadequate as compared to those which might be used in the future.

Hyperbaric recompression has been used in aviation and diving with remarkable success in the treatment primarily of the delayed "shock" syndrome and the neurologic manifestations of decompression sickness, but also of "bends" and "chokes" not relieved by descent (10, 13, 17, 21, 31, 40). It is apparent that in order to be maximally effective, this measure must be commenced as soon as possible after its requirement is recognized. In the past, United States Air Force



authorities have recommended that aviators requiring recompression be taken to a maximum "depth" of 6 atmospheres absolute, and decompression from this pressure be carried out in accordance with the standard United States Navy diving tables for the treatment of decompression sickness and air embolism. However, there is now both rational and empirical justification for the use of a recompression profile to a maximum "depth" of 3 atmospheres absolute with oxygen being breathed during recompression (40, 71). The theoretical bases for this are summarized in Table 4.1. It is pointed out that if experience justifies the use of such a profile for the treatment not only of manifestations of decompression sickness, but also possibly of other air embolic phenomena, the weight penalty associated with taking a recompression facility into space may be markedly diminished.

Characteristics	Standard Navy Treatment Tables	3 ATM. ABS. Oxygen Table
Maximal Pressure Applied	An amount of compression in excess of that needed for relief; limited by: Diminishing efficiency of added pressure to reduce bubble size; nitrogen narcosis; air density; heat of compression; risk of decompression sickness.	Limited by pressure-time aspects of O <sub>2</sub> toxicity risk and undefined retinal risk; Maximal bubble-ambient gradient for inert gas; Maximal efficiency of collateral circulation potential to supply compromised tissue foci.
Time of Exposure At Maximal Pressure	Pain unrelieved after 30 min. at depth not likely to be bends pain; symptoms persisting after 2 hr. probably herald residual tissue damage.	Not established; at least 1.5-2 hr. ; Oxygen toxicity protection from interspersed air-breathing periods being investigated for man.
Indications to Begin Ascent	Expiration of 30 min. period or 30 min. plus time to relief on Table 4 of Standard Navy Table.	Establish that remission is complete; Remain an additional arbitrary period unless ended by O <sub>2</sub> exposure concern.
Pressure-time Ascent Pattern	Decompression to 60 ft. rapid, limited by decompression sickness risk; stage ascent pattern with rapid pressure changes; 30 ft/12 hr. stage prevents new bends.	No risk of decompression sickness from treatment, slow pressure changes of continuous ascent maximize inert-gas elimination gradient and least disturb bubble nuclei, or cavitation-prone turbulent streams.
Respired Air	Usually compressed air deeper than 60 ft.; gradient for N <sub>2</sub> elimination postponed until O <sub>2</sub> stops; O <sub>2</sub> needed to prevent bends in Table 4 attendants.	O <sub>2</sub> primarily, to supply tissues harmed by occlusive bubble emboli, to assist inert-gas elimination from bubbles; not required to avoid bends from the treatment.

Table 4.1 Summary of recompression method characteristics and their theoretical bases.

(After Goodman (40))

The question is raised as to whether or not to recommend the instal-

lation of a recompression facility on board future spacecraft for the treatment of decompression sickness, air-embolic phenomena associated with meteoroid penetration (Chapter 12), explosive decompression (Chapter 3), and the ebullism syndrome (Chapter 2). Assuming that suitable spacecraft cabin atmospheres will be selected, current predictions fortunately indicate that the probability of serious manifestations of decompression sickness occurring during space operations will be extremely low <sup>(81)</sup>. It is also thought that other unforeseen events which could result in serious manifestations due to bubble emboli are potentially rare. Therefore, in the light of the predicted rarity of serious clinical problems due to bubble embolic phenomena in space, transporting a recompression chamber into space does not appear justified at the present time. However, it is considered possible that in the future, recompression facilities such as reinforced, appropriately equipped air locks which offer a minimum weight penalty might be placed in spacecraft, and space, lunar and planetary stations when large-scale extravehicular operations are to be carried out and significant risks of such problems occurring are anticipated.

Any plasma loss associated with decompression sickness must be immediately replaced, using either plasma or another suitable plasma-expanding agent such as dextran. A vasopressor or intravenous saline solution would be inappropriate for treating impending or manifest "shock", but should be used until a plasma-expanding agent is made available or if such an agent is not available. The volume of plasma requiring replacement might be determined by calculating the static plasma deficit. If pulmonary edema is part of the clinical picture, it would be wise to administer a plasma-expanding agent slowly to avoid aggravation of this condition. Successful therapy of plasma loss is indicated by the level and stability of the pulse rate and systemic arterial pressure, by repeated determination of the hematocrit and by a steady urine output of at least 30 ml per hour.

The question arises as to whether or not mannitol or another suitable osmotic diuretic should be administered in conjunction with a

plasma-expanding agent to an astronaut who suffers the delayed "shock" syndrome. As pointed out in Chapter 1, mannitol has been used effectively for the prevention of acute renal failure from a variety of hypoxic factors, and for the treatment of post-hypoxic cerebral edema. Therefore it should be administered prophylactically for renal failure to an astronaut who progresses to the "shock" stage of the delayed "shock" syndrome. Also conceivable is the possibility that mannitol might be used effectively to reduce and possibly reverse the diffuse extravasation of plasma which is characteristic of this syndrome. By the same token, mannitol might even be an effective form of treatment for the neurologic manifestations of decompression by reducing the focal embolic brain edema which presumably accounts for such manifestations. It must be pointed out, however, that the possible usefulness of this or any other therapeutic agent in the therapy of decompression sickness remains to be established.

Total body hypothermia has apparently been effective in the treatment of the neurologic manifestations of decompression sickness <sup>(35)</sup>. As was pointed out in Chapter 1, hypothermia reduces tissue oxygen demand, assists in the control of cerebral edema, and controls the hyperpyrexia so often associated with severe brain damage. Although hypothermia might be a valuable therapeutic measure for neurologic manifestations and perhaps the delayed "shock" syndrome of decompression sickness, rendering an afflicted astronaut hypothermic might be impossible to accomplish in space in the foreseeable future. It is conceivable, however, that adequate total body cooling might be attained with a space suit water-cooled garment. Recommended hypothermic levels are given in Chapter 1. Suppression of shivering would be possible with chlorpromazine.

Most authorities have recommended that 100 percent oxygen at ground level ambient atmospheric pressure be administered as indicated to cases suffering from the delayed "shock" syndrome of decompression sickness (1, 31, 32, 53). It has been suggested, however, that the cere-

bral vasoconstrictor effect of a high partial pressure of oxygen might in fact seriously compromise blood flow to brain tissue which has already been rendered ischemic by a combination of embolic blockage of blood flow and reflex irritative vasospasm<sup>(10, 90)</sup>. Because of its potent cerebral vasodilating action, 3.5 percent carbon dioxide has been added to high oxygen atmospheres, but the greater effectiveness of such gas mixtures over 100 percent oxygen in the treatment of the delayed "shock" syndrome, or even the neurologic manifestations of decompression sickness, remains to be proven<sup>(90)</sup>. Moreover, it should be remembered that currently proposed spacecraft cabin atmospheric pressures will not provide oxygen at a partial pressure which can significantly reduce cerebral blood flow. This would even be the case if an intravehicular astronaut is pressurized in his space suit.

Other therapeutic measures should be carried out as dictated by the particular case of decompression sickness. The intravenous administration of a rapid-acting cardiac glycoside, such as digoxin, might be considered if there is evidence of embolic myocardial damage or right heart strain secondary to embolic blockage of pulmonary blood flow or pulmonary edema. A sedative, such as phenobarbital, might be required to control an agitated astronaut. If an osmotic diuretic has been used, an electrolyte solution might be given intravenously to replace fluid and electrolytes, which are characteristically lost in excess as a result of osmotic therapy. Intravenous feeding might also be required. A clear airway must be insured by whatever means possible.

Finally, it should be mentioned that the potential usefulness of heparin in the treatment of decompression sickness remains to be determined. Whether or not this drug provided beneficial effects in animal decompression experiments through its anticoagulant, proteolytic or lipemia-clearing activity remains unanswered. The solution of this problem may lead not only to a better understanding of the basic mechanisms underlying the serious manifestations of decompression

sickness, but also to the possible discovery of agents which might be potentially useful in the treatment of decompression sickness in space.

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## CHAPTER 5

### AEROTITIS MEDIA AND AEROSINUSITIS

Aerotitis media and aerosinusitis are well known, occasionally incapacitating medical problems which result usually from an elevation of the ambient atmospheric pressure. Their occurrence during routine operations in space is considered unlikely; any cases will probably be attributed to certain predisposing factors. Since there has been a vast amount of detailed writing in this area, the discussion which follows will be brief, citing major works and presenting information which is pertinent only to missions in space.

#### Aerotitis Media

The generally accepted definition of aerotitis media was originally stated by Armstrong and Heim <sup>(2)</sup> as: "an acute or chronic traumatic inflammation of the middle ear caused by a pressure differential between the air in the tympanic cavity and that of the surrounding atmosphere". The non-infectious character of this condition must be emphasized, for only in very rare instances is infection a secondary complication (14, 25, 27, 33, 35, 39).

#### Pathophysiology

An astronaut might fail or be unable to open voluntarily one or both Eustachian tubes and so provide adequate middle ear ventilation during a recompression in space. Pressure in the middle ear might then become sufficiently negative relative to that of the ambient atmosphere to traumatize tissues surrounding this "semi-rigid" cavity. For all practical purposes, positive pressure differentials, even during "explosive" decompressions in space, should not be great enough to produce damage, provided that astronauts' Eustachian tubes have reasonably normal patency (1, 14, 33).

The anatomy and physiology of the Eustachian tube has been discussed in detail by many authors (1, 14, 24, 26, 32). Pertinent to this discussion is the fact that the tube has a flutter valve action which

opposes the passage of air from the nasopharynx into the middle ear cavity unless the tube is opened by contraction of its dilator muscles. This must be accomplished voluntarily by various acts such as swallowing, yawning, grinding movements of the lower jaw or the Valsalva maneuver. It is apparently impossible for these muscles to overcome a negative pressure differential of more than 80 to 90 mm Hg. (1, 2).

Either failure or inability of an astronaut to open the Eustachian tube during recompressions in space might occur under a variety of circumstances. A rapid recompression may not allow sufficient time or he might be too preoccupied to perform an adequate equalizing maneuver. Notably, maximum negative pressure differentials developed in the middle ear on recompressions from the present space suit atmospheric pressure of 3.7 psia (191 mm Hg) to possible spacecraft cabin atmospheric pressures of either 5.0 psia (259 mm Hg) or 7.0 psia (362 mm Hg) will be such that the astronaut should be only able to equalize immediately after recompression to 5 psia. Rapid emergency recompression modes which follow large decompressions of either space suit or spacecraft cabin might also lead to excessive negative pressure differentials. Inability to perform the highly effective Valsalva maneuver while in a "closed" space suit will undoubtedly be a factor predisposing to middle ear trauma from rapid suit or suit to cabin recompressions. Finally one should keep in mind that an unconscious astronaut and probably most semi-conscious astronauts will be incapable of equalizing.

The question arises as to whether a common cold or any other non-specific acute or chronic upper respiratory infection predisposes to aerotitis media. Such a condition might produce inflammatory swelling, especially in and around an otherwise normal Eustachian tube, sufficient to impair tubal function. A positive correlation between the incidence of aerotitis media and both the size of the adenoid and the presence of lymphoid tissue has been noted, but the magnitude of this relationship did not allow accurate prediction in individual cases (31). The role of infection could not be separated from that of lymphoid tissue in obstruction of the Eustachian tube (14). Extensive studies on

flying and diving personnel have failed to reveal a significant correlation between the incidence of aerotitis media and upper respiratory infections (11, 16, 17, 33). Another study even added the number of individuals excused from altitude chamber operations because of severe upper respiratory infection to the number who suffered from aerotitis media, but still failed to establish a definite relationship (33). The possibility that an astronaut might experience increased difficulty in ventilating his middle ears if his nasopharynx becomes inflamed cannot be denied, however. Accordingly, an upper respiratory infection might predispose to aerotitis media under certain circumstances in space, such as a rapid recompression or inability of an astronaut to perform the Valsalva maneuver during recompression.

So-called "secondary" or "delayed" aerotitis media can be caused by the absorption of oxygen from the middle ear; increase of the atmospheric pressure per se does not play a causative role (1, 4, 14, 27, 38). It usually appears in aviators who have breathed oxygen during descent and have failed to ventilate their middle ears adequately after descent, and is attributed to the effect of a high pressure gradient for oxygen being established between the middle ear cavity and the well perfused, metabolically active tissues of the middle ear. Clinical manifestations due to development of negative pressure in the middle ear usually appear some 2 to 6 hours after descent, in most cases while asleep during which the frequency of swallowing, and therefore of equalizing is reduced (1). Also of note is the fact that the absorption of oxygen can aggravate aerotitis media caused by an atmospheric pressure change (14).

Astronauts will undoubtedly run a risk of developing "delayed" aerotitis media after being recompressed in 100 percent oxygen from a space suit atmospheric pressure of 3.7 psia (191 mm Hg) to a spacecraft cabin atmosphere containing 50 percent nitrogen and 50 percent oxygen at a total pressure of 7.0 psia (362 mm Hg). The risk following suit recompression to a 100 percent oxygen atmosphere at 5.0 psia (259 mm Hg) should be essentially no different than that for continuous exposure to such a cabin environment. It has been shown that the continuous



absorption of oxygen from the middle ear (commonly referred to as "aural atelectasis" if no signs of aerotitis media are present) while living in this atmosphere is sufficiently rapid to cause discomfort after a period of several hours of sleep <sup>(12, 13)</sup>. Equalizing maneuvers were successful, so that "delayed" aerotitis media did not develop. Prolonged exposures to oxygen atmospheres at other pressures have presented a similar picture <sup>(19, 20)</sup>. Therefore, even though aural atelectasis commonly occurs in pure oxygen atmospheres, it appears from experience to date that there may be only a remote risk of serious "delayed" aerotitis media from exposure to such atmospheres during space missions.

The probable sequence of events responsible for producing the clinical picture of aerotitis media has been determined from animal experiments <sup>(7, 11)</sup>. The pathologic changes in the middle ear appear to be primarily vascular in nature, for some degree of hyperemia is nearly always present both in the tympanic membrane and in the mucosa of the middle ear. Mucosal edema and hemorrhage may occur singly or together, the hemorrhagic areas varying from tiny petechiae to large, confluent areas <sup>(14)</sup>. These effects are probably caused by a combination of factors attributable to negative pressure. These factors include vasodilatation sufficient to produce a temporary vascular paralysis, a stagnation of tissue blood flow, imbalance of osmotic and hydrostatic forces between vessel and tissue fluids, a disruption of overdistended small vessels and the tearing apart of mucosal and fibrous tissue layers. As this condition progresses, a non-inflammatory sterile fluid transudate appears in the middle ear cavity; there may even be gross hemorrhage <sup>(30, 36)</sup>. Since fluid and blood are space filling, the negative pressure differential decreases and consequently the progression of pathologic changes is arrested. Although the transudate and blood in the middle ear cavity are usually completely reabsorbed, blood in middle ear tissues can organize and hence possibly lead to some degree of permanent hearing loss.

It has been reported that at about a 200 mm Hg negative pressure

differential, the tympanic membrane may disrupt <sup>(1)</sup>. However this event apparently occurs at this level of pressure only in individuals with previous tympanic membrane disease, so that the critical pressure of a normal tympanic membrane might be considerably higher <sup>(1, 28)</sup>. Although negative pressure differentials sufficient to produce disruption will probably not be attainable during the space suit to spacecraft cabin recompressions in space discussed above, it is apparent that such pressures might be reached during large emergency recompressions of either the space suit or spacecraft cabin.

### Clinical Manifestations

Aerotitis media may be acute or chronic, unilateral or bilateral and mild or severe, depending on the degree and frequency of pressure differential insults on the ear. The incidence of monaural or binaural involvement is often about equal, although in monaural cases, signs of trauma from negative pressure are usually noted in the other asymptomatic ear <sup>(15, 16)</sup>. The clinical manifestations of acute aerotitis media may begin during or immediately following recompressions <sup>(1)</sup>. Symptoms of "delayed" aerotitis media usually appear some 2 to 6 hours after recompression while breathing oxygen.

The negative pressure which develops in the middle ear during recompression produces discomfort in the involved ear, then pain which may radiate to the temporal region, cheek, and parotid gland on the affected side <sup>(1)</sup>. The pain occurs usually when the pressure differential reaches 100 mm Hg and is usually stabbing in character; it can begin gradually or suddenly and vary from mild to unbearable <sup>(1)</sup>. Its intensity does not necessarily parallel objective findings, for afflicted individuals have complained of severe pain and yet on examination were found to have no changes indicating the presence of aerotitis media <sup>(34)</sup>. Conversely, slight or even no pain has been reported in instances of tympanic membrane disruption <sup>(23)</sup>. Pain is usually relieved on early ventilation of a mildly traumatized middle ear.

More severe trauma is followed by a sense of soreness in the ear and an occasional sharp pain caused by movement of the inflamed tympanic membrane <sup>(1)</sup>. Disruption of the tympanic membrane is accompanied by a sharp piercing pain, a loud "explosive report" which is felt and heard in the affected ear; associated vertigo and nausea may persist for many hours. With disruption, acute pain quickly subsides, but a dull ache may remain for up to 2 days.

Partial deafness is the most frequent complaint of individuals suffering from aerotitis media <sup>(14, 23, 27)</sup>. A conduction type of hearing loss of up to 15 to 30 decibels can persist from a few hours to many days in duration, depending mainly on such factors as the degree of immobilization of the tympanic membrane by a persisting pressure differential and by edema and blood which accumulates in the membrane, and whether a fluid transudate or blood accumulates in the middle ear cavity <sup>(1, 10, 15, 31)</sup>.

This loss may be fairly uniform for the various frequencies or may in certain individuals affect principally the lower or the higher frequencies <sup>(1, 27)</sup>. In general, hearing for the lower frequencies seems to be depressed first, and as more fluid is drawn into the middle ear cavity, the high frequencies become more and more effected <sup>(27)</sup>. It is noted that permanent perceptive type of deafness may rarely occur, presumably due to labyrinthine hemorrhage <sup>(10)</sup>.

There are always temporary sensations of "fullness" and "stiffness" in an involved ear <sup>(27)</sup>. These symptoms are often accompanied by a feeling of fluid in the ear <sup>(14)</sup>. Tinnitus occurs infrequently. Vertigo is also uncommon; when present, it is usually unilateral <sup>(18)</sup>. Bubbling sounds may be heard on blowing the nose, swallowing or yawning <sup>(27)</sup>. Another symptom which occasionally appears is autophony, in which the individual's own voice and breathing sounds unusually loud to him <sup>(1, 27)</sup>.

The appearance of the tympanic membrane in aerotitis media often, but not always correlates with symptoms of this condition fairly closely <sup>(14)</sup>. A classification of progressive pathologic changes

visualized on otoscopy has been advanced by Teed <sup>(34)</sup>, and is somewhat altered here to correspond with the excellent account of otoscopic findings presented by Armstrong <sup>(1)</sup>. It is noted that the tympanic membrane may or may not be retracted at the time of otoscopic examination.

Grade 1 - injection of the blood vessels running over the pars flaccida and along the handle of the malleus. At a more advanced stage, there is erythema of the upper and posterior portion of the tympanic membrane.

Grade 2 - redness of the entire tympanic membrane and adjacent portions of the external auditory canal. The tympanic membrane develops a translucent appearance, and small droplets of fluid may be seen on its medial surface.

Grade 3 - gross fluid and bubbles in the middle ear; this may be temporarily concealed by congestion and edema of the tympanic membrane.

Grade 4 - hemorrhage into the substance of the tympanic membrane and/or into the middle ear; this may be temporarily concealed by congestion of the tympanic membrane. If it occurs, a traumatic rupture of the tympanic membrane will usually be linear, quite extensive, and may involve any portion of this structure; the margins of a fresh rupture are red, the whole tympanic membrane is intensely inflamed and there is usually a small amount of blood in the external auditory canal.

Acute aerotitis media has generally a good prognosis, provided that treatment is adequate and sufficient time is allowed for complete recovery <sup>(14)</sup>. The recovery period may vary from a few hours to 3 or 4 weeks in duration. Both the rapidity with which treatment is initiated following exposure and the type of treatment employed may affect the prognosis. As mentioned above, middle ear infection is a very uncommon complication of acute aerotitis media.

Finally, it should be pointed out that repeated insults on the middle ear can lead to a chronic form of aerotitis media <sup>(1, 37)</sup>. This is probably caused by a partial stenosis of the Eustachian tube preventing adequate pressure equalization <sup>(1)</sup>. Symptoms are aggravated by

repeated recompression, and include continuous feelings of "fullness" and "stiffness", occasionally tinnitus, and rarely pain in the affected ear. Whether hearing acuity is diminished in this condition is not known, but it has been observed that atmospheric pressure changes are capable of producing permanent injury to both the middle ear and cochlea portion of the middle ear (1, 37). Signs of chronic aerotitis media include a dull, lusterless and slightly thickened tympanic membrane, and a diminished or absent light reflex (1).

### Diagnosis

History of recompression exposure and the associated appearance of symptoms and otoscopic findings discussed above usually make the diagnosis of aerotitis media easy. Asymptomatic injection of vessels in the tympanic membrane can appear in association with upper respiratory tract disease, after performing the Valsalva maneuver and in 50 percent of all individuals exposed to large rapid recompressions (1, 33). However, the presence of only Grade 1 changes and the absence of symptoms in these situations should allow differential diagnosis.

### Prevention

Normal upper respiratory passages, middle ears and Eustachian tubes, and a proven capability to equalize during reasonably rapid recompressions by the simple maneuvers, such as swallowing, yawning, or grinding movements of the lower jaw, are prerequisites for astronaut selection. It is important to note again that the astronauts are unable to perform the Valsalva maneuver while in a "closed" space suit.

If difficulty with equalization occurs during recompression from a space suit to spacecraft cabin atmospheric pressure, adequate voluntary control might be attained by decompressing to a pressure which provides relief, then by recompressing more slowly. However, in an emergency recompression, an astronaut who cannot equalize will have to suffer the consequences of having a negative pressure develop

in one or both of his middle ears.

An astronaut with an upper respiratory infection should if possible avoid decompression-recompression operations. As noted above, an inflammatory reaction in and around the Eustachian tube might predispose to difficulty in ventilating the middle ear, especially if he is unable to perform the Valsalva maneuver. Prophylactic administration of a topical or oral decongestant agent to be mentioned below might be considered. Even though this procedure was unsuccessful in two large scale studies, more potent and specific drugs are presently available (21, 31). This area therefore requires further study.

"Delayed" aerotitis media after recompression to an atmosphere containing an inert gas can be prevented by ventilating the middle ear, especially if a sleep period is soon to follow. Armstrong <sup>(1)</sup> suggests that adequate ventilation can be accomplished by performing about six reverse Valsalva maneuvers (taking a mouthful of water, holding the nostrils closed and swallowing). If there is a risk of "delayed" aerotitis media from living in a 100 percent oxygen environment, no preventive measures can be suggested other than short sleep periods, periodic equalization (even though no requirement might be felt), and optimum hydration to promote adequate salivation and thus frequent Eustachian tube opening through swallowing.

### Treatment

The majority of cases of acute aerotitis media in aviators are mild, requiring either no therapy or minimum conservative therapy (1, 14, 27). This should not be taken to mean, however, that a similar situation will always exist in space, for failure of highly experienced astronauts to equalize will probably in most instances result from the predisposing events discussed above, and could lead to serious cases of aerotitis media unless negative pressure differentials are immediately equalized.

Relief of negative pressure in the middle ear may be attempted

first by shrinking the nasal mucous membrane, including that in around the Eustachian tube orifice, with a suitable vasoconstrictor or decongestant spray, such as 1/1000 epinephrine, or oral preparation, such as pseudoephedrine or triprolidine. The Valsalva maneuver should then be performed again. If this attempt at equalization fails, inflation of the Eustachian tube might be tried with a technique which uses air delivered at a controlled positive pressure, if such is available in space, according to the same principles as politzerization (14, 21, 22, 23). The control valve should be set initially to deliver a pressure of 20 mm Hg and if this is not sufficient to provide relief, this pressure can be raised by 5 or 10 mm Hg increments (14).

Paracentesis or myringotomy should be performed only in cases which fail to respond to methods of vasoconstriction and inflation. They are highly skilled procedures which demand extreme care to avoid implanting infectious organisms into a culture medium which would otherwise remain sterile (1). Cleansing and sterilization of the external auditory canal and tympanic membrane might be accomplished with an antiseptic agent such as hexachlorophene on a cotton-tipped applicator. Local anesthesia is ineffective. Paracentesis is the procedure of choice. Aspiration of transudate or blood from the middle ear cavity should be carried out when indicated, for it appears to hasten recovery and may prevent the formation of adhesions with subsequent permanent hearing impairment (1, 14, 27, 36). If only paracentesis is to be performed, a short-bevel 22 gauge needle might suffice. If aspiration is indicated, a double-barreled paracentesis needle, which allows a compensatory passage of air into the middle ear while fluid is being withdrawn, should be used (29). Myringotomy might be performed with a larger needle or a myringotomy knife. The prophylactic administration of a systemic antibiotic might be indicated following either of these procedures.

Catheterization of the Eustachian tube is not a recommended procedure to be attempted in space. The most important objection to it is the great possibility of producing serious permanent damage to

the tissues at the Eustachian orifice (9, 14, 27).

Other possible therapeutic requirements include a suitable analgesic or sedative for the control of pain, and an antibiotic for secondary infection.

A ruptured tympanic membrane requires no specific treatment, unless secondary infection occurs <sup>(1)</sup>. Except in emergency situations, decompression-recompression maneuvers should not be carried out until healing is complete.

### Aerosinusitis

As on Earth, the potential incidence of aerosinusitis in space will probably be much less than that of aerotitis media <sup>(1, 6)</sup>. Therefore this clinical entity will be discussed only briefly here.

Aerosinusitis is also acute or chronic inflammation caused by a pressure differential, usually negative, but in this case existing between a semi-rigid nasal cavity, or nasal sinus, and the ambient atmosphere <sup>(6)</sup>. Usually only one sinus is involved - the frontal most frequently, then the maxillary sinus and rarely the ethmoid sinus <sup>(1, 6, 8)</sup>.

The pathophysiologic mechanisms responsible for producing aerosinusitis have been elucidated by Campbell <sup>(5, 6)</sup>. Aerosinusitis in an otherwise normal nose is most commonly due to inflamed tissue blocking a sinus ostium or, in the case of the frontal sinus, the duct connecting the nasal cavity with the sinus. This tissue has a ball valve effect in that air is allowed good exit into the sinus but poor entry during pressure change. This effect is undoubtedly enhanced by viscous sticky secretions in the area. The pathologic changes which can be produced by a negative pressure differential in a sinus are similar to those described previously for aerotitis media. Of note, however, is the fact that infection appears to be a common complication of aerosinusitis, in most cases no doubt due to either an extension of the infection which caused the blockage,



or infection already existing in a sinus.

Readily apparent factors predisposing to aerosinusitis include upper respiratory infection involving the nasal mucous membrane and rapid recompression if partial stenosis of an ostium or duct exists. Aerosinusitis as a consequence of living in a 100 percent oxygen environment has not been described, but is considered possible.

Clinically, aerosinusitis is characterized by persistent pain which often begins suddenly and is usually localized over the affected sinus (1, 6). Lacrimation can occur (1). Infection of a sinus may be accompanied by severe throbbing pain, and possibly fever and general malaise. Nasal bleeding might follow severe trauma to the sinus mucous membrane (5). On examination, local tenderness can often be elicited over the affected sinus, and redundant tissue and a purulent discharge might be seen about the sinus opening.

The most important measure preventing the occurrence of aerosinusitis in space is obviously the selection of astronauts with normal nasal and sinus cavities and most particularly, adequate sinus openings. Other preventive measures are those which were discussed for "Aerotitis Media".

The treatment of aerosinusitis is directed at the relief of the obstruction with an appropriate decongestant, the control of pain and the treatment of concurrent or secondary infection (1, 5, 6).

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## CHAPTER 6

### HEAT DISORDERS, INCLUDING DEHYDRATION

The heat disorders are clinical manifestations of disordered physiology resulting from the imposition of an excessive heat load on the body. The heat load may be either metabolic or environmental heat, or both.

The most likely cause of any heat disorder suffered in space is thought to be an inadequacy or failure of the temperature control system of a space suit during an extravehicular operation. However, even with the highly effective temperature control systems currently being developed for space suits, it is thought that there will still be a risk of a heat disorder occurring during future space missions <sup>(30)</sup>.

This chapter very briefly discusses various aspects of the heat disorders considered pertinent to the space situation. Greater detail on these disorders can be obtained from the excellent reviews of Leithead and Lind <sup>(24)</sup>, Minard and Copman <sup>(27)</sup>, Webb <sup>(33)</sup> and other literature to be cited here.

#### Classification

The classification of the heat disorders presented by Leithead and Lind <sup>(24)</sup> is well oriented from a clinical standpoint. It outlines these disorders in terms of cause, and points out that signs and symptoms associated with the physiologic compensatory mechanisms are just as much heat disorders as are the clinical manifestations caused by the actual failure of thermoregulation. This classification follows:

1. The disorders which result from, and may complicate the processes of thermoregulation:
  - a) Due to circulatory instability - heat syncope.
  - b) Due to water and electrolyte imbalance - heat edema, water-depletion heat exhaustion, salt-depletion heat exhaustion, heat cramps.
  - c) Due to skin changes - prickly heat, anhidrotic heat exhaustion.
2. The disorders which result from failure of thermoregulation: heatstroke, heat hyperpyrexia.
3. The disorders which are characterized by apathy

or fatigue, or deterioration in the performance of skilled tasks without any evidence of the entities listed above: acute heat fatigue.

It should be kept in mind that one or more of the above heat disorders can be suffered at the same or different times, during or after exposure to a heat load. Since many heat disorders share common clinical manifestations, an accurate diagnosis in the absence of certain laboratory measures might be difficult. Fortunately, however, most of them respond rapidly to the same treatment.

### Clinical Manifestations

#### Heat Syncope (Heat Collapse, Heat Prostration, Heat Exhaustion).

Heat syncope characteristically follows sudden exposure to a severe heat load. Although some degree of water depletion may play a role in its genesis, this syndrome has been attributed primarily to heat-induced peripheral vasodilatation which leads to systemic arterial hypotension<sup>(33)</sup>. The associated deficiency of cerebral blood flow might be indicated at first by lightheadedness or dizziness. Acute fatigue, restlessness, nausea and blurring of vision might also precede syncope, and may be severe enough to render the afflicted individual incapable of undertaking a life-saving action. Rectal temperature is usually not significantly elevated, unless the individual who suffers heat syncope has been exercising.

Heat syncope is more apt to occur in individuals who are unused to heat or the combined stresses of heat and work<sup>(33)</sup>. It would probably not be expected to occur in physically fit astronauts, especially if they are repeatedly exposed to the range of thermal conditions expected in emergency situations in space<sup>(33)</sup>.

In the weightless environment, syncope provoked by a sudden postural change should not occur. For this reason, syncope in this environment will probably be a manifestation of a more serious circulatory impairment than syncope while sitting or standing in the gravity environment. As was pointed out in Chapter 10, both simulation studies to determine how the body responds to weightlessness and experience to date in space indicate

that prolonged exposure to weightlessness will lead to a temporary, and possibly a permanent decrease of blood volume. This and other cardiovascular adaptations to weightlessness appear to enhance the tendency to orthostatic tolerance (Chapter 10). Hence one would expect that cardiovascular adaptations to weightlessness would increase an astronaut's susceptibility to the hypotensive effect of heat stress imposed either during operations in a gravity environment, such as while exploring a lunar or planetary surface, or when accelerative forces are applied in the head-to-foot direction during landing and take-off operations. The various methods under study for assuring normal orthostatic tolerance on return to a gravity environment are discussed in Chapter 10.

#### Heat Edema

This condition usually is a trivial consequence of a prolonged exposure to heat. Mild edema usually occurs in the feet. Since the gravitational component of intravascular hydrostatic pressure determines its production and distribution on Earth, heat edema may not occur in space. However, it is possible that mild venous occlusion produced by garment cuffs around extremities could predispose to heat edema, especially if an astronaut must endure a heat load for a prolonged period of time. This condition conceivably might develop after prolonged extravehicular activities in a gravity environment.

#### Water-Depletion Heat Exhaustion (Water-Deficiency Heat Exhaustion, Dehydration).

Water-depletion heat exhaustion, more commonly referred to as "dehydration", results from failure to replace body water, lost in this case by sweating, through the inability to find or ensure an adequate intake of fluids. A "space-oriented" review of pertinent literature in this area has recently been completed by Webb<sup>(33)</sup>. Other information can be obtained from the major references cited in this chapter.

Signs and symptoms of dehydration have been summarized in chart form, as shown in Figure 6.1. It is important to note that such clinical manifestations, especially fatigue, can appear quite suddenly and with such severity as to lead to a serious decrement in task performance. One must also keep in mind that, as military experience in hot climates has shown, small amounts of dehydration can easily become cumulative if continued day after day.

Of interest is the well known fact that men working in heat fail to drink back water as fast as it is lost. Attempts to do so often lead to feelings of nausea and abdominal distension<sup>(33)</sup>. This phenomenon, referred to by various authors as "mild dehydration", "voluntary dehydration", "voluntary under-drinking", and "involuntary hypohydration", can lead to water depletion which may amount to one to two percent of the initial body weight<sup>(7, 18, 22, 33)</sup>. Dehydration due to voluntary under-drinking does not usually produce clinical manifestations. However, a clinically overt disorder can result from a sudden further demand placed on the body's water stores.

A connection between orthostatic intolerance and mild dehydration has been established<sup>(1, 6)</sup>. As would be expected, a markedly exaggerated orthostatic response is produced by a combination of dehydration, mild elevation in body core temperature, and bed rest, the latter supposedly producing the circulatory effects which can occur in the weightless environment (Chapter 10). Again the potentially disastrous effects of allowing such a combination of stresses to act on an astronaut, especially in a gravity environment during a space mission, are readily apparent.

#### Salt-Depletion Heat Exhaustion

This condition is due to the inadequate replacement of sodium chloride lost usually in prolonged sweating. It may occur even if fluid replacement is adequate.

Salt-depletion heat exhaustion is characterized mainly by fatigue. However, other signs and symptoms which can appear are dizziness, anorexia, nausea, vomiting, headache, mental confusion, muscle cramps,



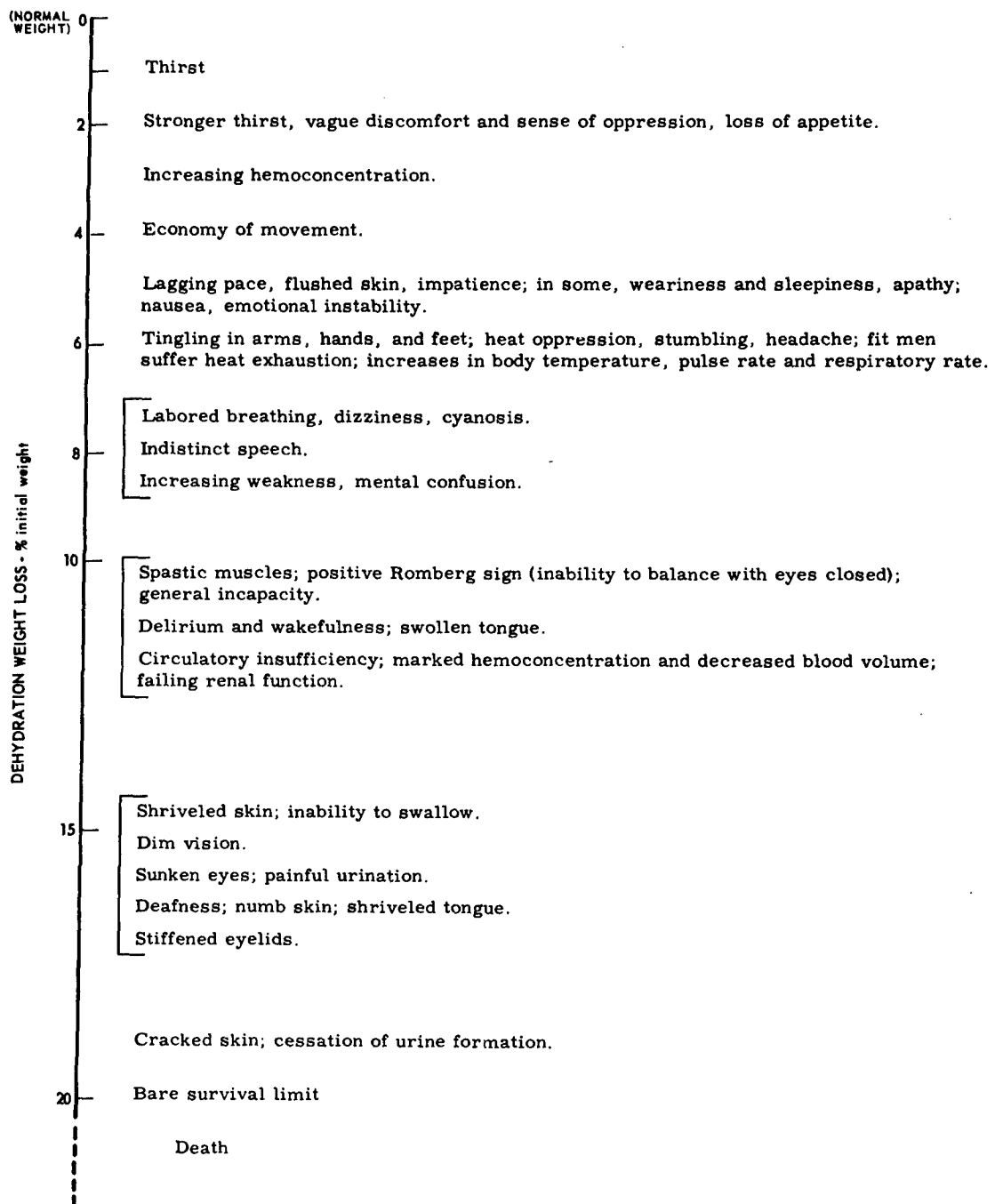


Figure 6.1 Dehydration.

(After Webb <sup>(33)</sup>).

constipation or diarrhea. Severe cases can progress into "shock", coma and death. The urine in all but the late stages of this syndrome is of reasonable volume, but contains negligible amounts of sodium chloride.

The plasma sodium concentration is decreased.

In contrast to water-depletion heat exhaustion, this syndrome characteristically tends to begin slowly, producing milder, more chronic symptoms <sup>(24)</sup>. Recognition of salt-depletion heat exhaustion is usually difficult, and hence its treatment tends to be delayed.

Water and salt-depletion heat exhaustion usually co-exist, the one or other possibly predominating, but both requiring treatment <sup>(24)</sup>. Moreover, by specifically treating the one disorder, it is possible to make the other manifest clinically. From the above considerations, an astronaut with a presumably adequate dietary sodium intake will more likely experience primarily water-depletion heat exhaustion.

### Heat Cramps

Heat cramps are painful spasms of voluntary muscles. They are usually associated with hard physical work in a hot environment. The causative factor appears to be intracellular overhydration <sup>(24)</sup>. This can apparently result from either primary salt depletion or the replacement of sweat losses with unsalted water. The cramps may occur during or after exposure to a heavy work load. There are no prodromal symptoms. A typical cramp lasts about 30 seconds and then relaxes spontaneously. It is noted that the pain and muscular spasm of a heat cramp could conceivably be severe enough to incapacitate an astronaut temporarily.

### Prickly Heat (Heat Rash, Miliaria)

This well known skin condition appears to result mainly from prolonged wetting of skin by sweat, as in a hot humid environment. It is apparently due to blockage of sweat gland ducts by keratin debris and edematous epithelium <sup>(24)</sup>. Associated symptoms can be annoying or be severe enough to disable the afflicted individual.

Prickly heat characteristically commences as many small discrete red papules on a mildly erythematous skin. These papules may develop into tiny vesicles which contain a clear or milky fluid, each surrounded by an erythematous area. In long-standing cases, the vesicles might become secondarily infected, forming pustules <sup>(19)</sup>. Hence, untreated

prickly heat can progress into an infected eczematous skin reaction.

Prickly heat is particularly prone to develop in skin creases where sweat collects and is poorly evaporated (e.g., axillae, front of elbows, groins, back of knees), or in areas where clothing exerts pressure, prevents adequate sweat evaporation, or chafes the skin (e.g., waist, sternum, back, shoulders, neck). It produces a sensation which is usually described as an intense prickling or tingling that comes on in waves and is triggered by an increase in sweating, by a sudden movement or by contact with clothing <sup>(24)</sup>. Severe itching and burning sensations are also common. It is readily apparent that this condition could seriously impair an astronaut's performance by producing sleep loss or severe distraction during critical work periods. The question as to whether prickly heat could lower the threshold for symptoms from radiation to skin in space (Chapter 11) remains to be answered.

The occurrence of prickly heat will be highly unlikely in a comfortable "shirt-sleeves" spacecraft cabin environment. On the other hand, it might conceivably result from prolonged operations in an inadequately ventilated, excessively warm space suit.

#### Anhidrotic Heat Exhaustion

Anhidrotic heat exhaustion affects individuals who are usually exposed for several months to a hot climate <sup>(24)</sup>. Hence this syndrome would be most unlikely to occur in space.

This condition is characterized by the appearance of numerous discrete vesicles, mainly in the skin of the trunk and proximal parts of the limbs, and by diminished or absent sweating (anhidrosis) in the areas covered by this rash. In anhidrotic heat exhaustion, there is not only a decrease in sweat delivery to the skin surface due to sweat gland blockage, but also a depression of sweat production. Vesicles in this condition are more deeply situated than, and may even co-exist with the vesicles of prickly heat <sup>(24)</sup>. There are usually no signs of dehydration, in spite of the fact that polyuria for an unknown reason occasionally occurs <sup>(24)</sup>. The concentration of sodium chloride in the sweat is usually

elevated.

The major symptom accompanying anhidrotic heat exhaustion is marked fatigue <sup>(24)</sup>. Palpitation and a sensation of oppression on exposure to heat are also experienced. Mild to moderate hyperthermia (100 to 102° F) has been observed. These symptoms usually subside rapidly on ceasing work and on exposure to a cool environment. Recovery of sweating is slow and heat tolerance may remain below normal for some time. As a rule, heatstroke does not follow, but must be distinguished from anhidrotic heat exhaustion.

#### Heatstroke (Heat Apoplexy, Hyperthermia, Heat Hyperpyrexia)

Heatstroke is characterized by a total absence of sweating, a self-perpetuating hyperthermia of usually 106° F or higher, and a severe disturbance of consciousness and brain function. Without treatment, this condition usually progresses on to death.

Very little is known about heatstroke, for as one of the most urgent of all medical emergencies, its immediate treatment has taken priority over its clinical investigation. Since it is associated with a high mortality, even when adequate cooling of an individual is carried out, this serious heat disorder cannot be induced for experimental purposes in man.

Heatstroke is not the usual response of man to extreme heat stress. The more common consequences which have been described above are, in contrast, characterized by continued sweating at reduced rates and a moderate or no elevation of body temperature. In a space flight context, there conceivably may be a situation where collapse results from combined heat stress and circulatory insufficiency without a remarkable rise in body temperature <sup>(33)</sup>. In this situation, the astronaut might be unable to take some life-saving action, so that if the heat stress continues, serious or fatal heatstroke might develop.

The pathogenesis of heatstroke is unknown. The question as to how much the decline in sweating is peripheral or central in origin remains to be answered <sup>(27)</sup>. Of note is the fact that the cessation of sweating and hence of the most important mechanism of body heat dissipation is permanent

unless heroic measures are undertaken to lower the body temperature.

A prodromal period of up to 5 days may precede heatstroke. Symptoms such as headache, dizziness, weakness, restlessness, syncope, nausea, vomiting, tachycardia, a feeling of oppressive heat, muscle cramps and dyspnea may occur (24, 33). The prodrome appears to belong to a category in which heat exhaustion with moderate hyperthermia is the underlying disorder. If this prodrome is recognized and adequately treated, heatstroke is prevented. More often, however, an individual has the prodromal period measured in minutes, especially if exposed temporarily to a severe heat load. In fact he can be essentially asymptomatic up to the moment he loses consciousness. Cessation of sweating involving the entire body, including the face and axillae, may be often noted immediately prior to the onset of heatstroke. Other signs and symptoms in this critical period are a flushed dry skin, an increase in the rate and depth of breathing, a growing restlessness, an inability to fix attention on any task, and frequently pallor around the eyes and lips (33).

The skin of an individual suffering from heatstroke is characteristically hot, dry, and flushed. On occasion it becomes cyanotic. The body temperature tends to be highest in those cases with the shortest prodromal period, thus indicating the potential seriousness of this condition and the need for heroic emergency medical measures. If the prodrome is prolonged, the temperature is usually less than 106° F. Central nervous signs and symptoms vary from mild confusion to delirium, convulsions, and coma. A direct relationship between the nervous manifestations and the degree and duration of hyperthermia is apparently always evident. Breathing is rapid and deep. Signs of "shock", such as pallor, cyanosis, hypotension, "thready" pulse and oliguria, are not seen until heatstroke is far advanced. This type of circulatory failure is considered to be predominantly peripheral in origin by Minard and Copman (27) and cardiac in origin (forward heart failure) by Gold (16). In spite of opposing views, however, treatment should probably be intensively directed at both causes of failure as "shock" usually heralds a rapid death. Except in those cases which

are preceded by severe heat exhaustion, hemoconcentration and changes in blood electrolytes are usually not seen in heatstroke. The state of acid-base balance during heatstroke remains to be determined. For a more detailed discussion of the clinical and pathologic findings in heatstroke, reference is made to the studies of Malamud and co-workers <sup>(26)</sup> and the review of Gottschalk and Thomas <sup>(17)</sup>. Reference is also made to the Army experiences with heatstroke in World War II, summarized by Schickele <sup>(31)</sup>.

An over-all mortality figure in the range of 15 to 25 percent in heatstroke would seem to be a reasonable estimate from past data <sup>(2, 23)</sup>, although Leithead and Lind <sup>(24)</sup> give a figure of 20 to 50 percent (average 35 percent). The majority of individuals who survive heatstroke usually recover <sup>(27)</sup>. Their body temperature usually remains unstable from 3 to 21 days, so that a strong predisposition for recurrence of heatstroke or other heat disorders exists during this time. A small percentage of individuals are chronically disabled to some degree by neurological lesions which most commonly involve the cerebellum (e.g., ataxia or motor incoordination, and dysarthria). Mental disturbances may range from those detected only by a special examination, to a complete change in personality or actual dementia <sup>(23)</sup>.

### Heat Hyperpyrexia

Heat hyperpyrexia is a term used in the classification of heat disorders by Leithead and Lind <sup>(24)</sup> to refer to a condition which differs from heatstroke in that the individual is still conscious and rational, and sweating is still present. The rectal temperature is usually above 105° F, but tends to be lower than in heatstroke. According to this definition, heat hyperpyrexia could conceivably represent either a form of heat exhaustion with hyperthermia, the prodrome of heatstroke, or a condition of hyperthermia following severe exercise. It is, therefore, a vague term which if not defined more specifically, might best be discarded.

### Acute Heat Fatigue

A decrement in the performance of skilled mental and physical tasks

tends to occur in unusually hot environments. The reason for this has not been given. It is not associated with any of the clinical manifestations listed above. The degree of impairment is influenced by such factors as motivation, type of task, degree of acclimatization to heat and physical condition. Many different kinds of performance can be affected, including those which depend principally on perceptual activities, on thought processes of differing complexity, and on sensorimotor coordinations of response mechanisms <sup>(24)</sup>. This problem is not considered to require treatment other than a reduction of environmental temperature to a tolerable level. For further detail on this problem, reference is made to Leithead and Lind <sup>(24)</sup>.

### Diagnosis

For the most part, the diagnosis of most heat disorders in space will be obvious from the history and physical examination of an affected astronaut. Special laboratory procedures such as determinations of serum and urine sodium concentrations, even if possible in space, should not be required unless the signs and symptoms force consideration of a differential diagnosis. Information concerning past fluid intake and urine output might prove valuable, particularly in the diagnosis of a disorder which begins slowly. Rectal temperature readings would be preferable, but oral readings might suffice. For features diagnostic of the various heat disorders, reference is made to the preceding brief discussions of those disorders and to the references cited.

### Prevention

The question arises as to whether or not an astronaut should be acclimatized to heat in anticipation of a possible exposure to an excessive heat load in space. Of great value in assessing the feasibility of this measure are the numerous writings cited in the following brief discussion of this area.

Acclimatization to heat is a qualitative and loosely used term referring to a complex physiologic response to an increased heat load. This response improves thermoregulatory processes, so that the potential harmful

effects of a heat load on the body are minimized and hence optimum body functioning is maintained. In spite of intensive investigation, the basic mechanism underlying acclimatization to heat has not been defined. Numerous studies have shown that with repeated exposures to an increased heat load, the thermal threshold for sweating and the concentration of salt in the sweat progressively decrease, and the maximum sweat rate progressively increases (1, 4, 5, 11, 13, 14, 20, 25, 29, 34). Concomitantly, the elevation of skin and rectal temperatures and the pulse rate during an exposure, and the expenditure of energy for a given work load become progressively less. Other physiologic parameters measured during the acclimatization process have been discussed by Leithead and Lind (24), Bass (3), Robinson (28), and Fox and co-workers (12, 15). The end result of acclimatization to heat is the loss of the characteristic subjective discomfort, lassitude, and impaired ability to work which affect the exposed, unacclimatized individual. As well, acclimatization markedly reduces the incidence of heat disorders.

Evidence is conclusive that this acclimatization process with its many physiologic variables behaves in many ways like a single physiologic response. Robinson and co-workers (29) clearly demonstrated the effectiveness of combining hard work with heat exposure to produce rapid acclimatization. The following characteristics of heat acclimatization, as presented by Bass (3), have been supported by many investigators (4, 5, 11, 25, 28, 29, 34).

Heat acclimatization begins with the first exposure to heat, progresses rapidly and is usually well developed in 5 to 9 days.

It can be induced by short, intermittent work periods in the heat lasting at least two hours daily. The general pattern of acclimatization is the same for short, severe exertion as for moderate work of longer duration. Inactivity in the heat usually produces only slight acclimatization.

Subjects in good physical condition usually acclimatize more rapidly and are usually capable of doing more work in the heat. Good physical condition, however, does not



in itself confer acclimatization.

The ability to perform "maximal" work in the heat is attained quickly by progressively increasing the work load within the capacity of the individual.

Acclimatization to severe conditions will facilitate performance at lesser conditions and provide "partial" acclimatization to more severe conditions.

Inadequate water and salt replacement can retard the acclimatization process.

Acclimatization to heat is well retained during periods of no exposure for about 2 weeks. Thereafter, it is lost at a rate which varies among individuals. The major portion is lost within 1 to 2 months. Maintenance of optimum physical condition promotes the best retention of acclimatization.

Is it practical to attempt prophylactic acclimatization of an astronaut to heat in order that he might better handle an unanticipated high heat load in space? Since the major portion of this acclimatization appears to be lost within 1 to 2 months, it would seem impractical to carry out this measure prior to a mission of this duration. On the other hand, it is conceivable that acclimatization to heat, and so the optimum use of sweating as a thermoregulatory response, could be maintained in space by subjecting an astronaut to repeated high work (exercise) loads in a warm environment such as an inadequately cooled space suit. This view has been supported by the reports of Blockley <sup>(7)</sup>, Roth <sup>(30)</sup> and Webb <sup>(33)</sup>. If such training were carried out, an astronaut would be prepared to take full advantage of a gas ventilating system during an extravehicular mission. Other advantages to acclimatization to heat would include a lessening of the susceptibility to circulatory insufficiency in situations involving some degree of heat load <sup>(33)</sup>. It is of interest to note that Fox and co-workers <sup>(14)</sup>, have reported success in acclimatizing individuals to heat by artificially elevating the body temperature. The role of physical condition in determining both the ability of an unacclimatized astronaut to handle a high heat load and the duration of retention of acclimatization must also be considered.

The requirement for acclimatization to heat will be greatly influenced by future evaluations of the risks of inadequacy or failure of temperature control systems under various conditions which might result in the exposure of an astronaut to a high heat load. Therefore, it appears that the practicability of acclimatization to heat will depend on a continued evaluation of risk. This will in turn depend for the most part on the reliability data from the future development and testing of temperature control systems, and on the type and duration of the mission.

Other preventive measures are readily apparent, for all must be taken to prevent heat disorders, whether on Earth or in space. The main measures include an adequate salt and water intake, and adequately functioning spacecraft cabin and space suit temperature control systems. Ideally, serious dehydration should be prevented by taking small amounts of water during the time the water loss is high. Drinking large amounts of water may produce diuresis with a net loss of body water <sup>(21)</sup>. As well, gastric distress and even vomiting - a very serious hazard in the weightless environment (Chapter 8) - may be provoked. If heat-stroke is suffered by an astronaut, he should not perform activity which could result in a heat load being forced upon him for at least 2 to 3 weeks.

Finally, it should be remembered that singly or combined, a loss of acclimatization, a decrement in physical condition, and a decrease in circulating blood volume on return to a gravity environment or due to voluntary under-drinking in space are factors which could seriously increase the susceptibility of an astronaut to heat stress and should, therefore, always be brought into consideration when the setting of normal and emergency tolerance limits to heat loads in space.

#### Treatment

The treatment of heat disorders has been discussed in detail by Leithead and Lind <sup>(24)</sup>, Minard and Copman <sup>(27)</sup>, and others (8, 9, 32, 33). With the exception of heatstroke, all heat disorders which could occur in space should be cured rapidly and completely if adequately treated.

Based on well established principles, treatment will usually include a period of rest in a cool environment and the replacement of depleted body salt and water. Rarely might it be necessary to use special measures to lower the body temperature or to treat "shock".

Heat syncope on Earth usually responds rapidly on exposing the afflicted individual to a cool environment. However, if heat syncope occurs in space it should be assumed that since there is no postural hypotensive effect in the weightless environment, the syncope has been contributed to by a decrease in blood volume due to one or more related or unrelated causes, such as voluntary under-drinking, excessive sweating, inactivity or weightlessness per se. This might mean that syncope in an astronaut exposed to a heat load should be considered a possibly serious "shock" state which should be treated intensively with intravenous fluids, a vasopressor and oxygen if the astronaut does not respond rapidly to a cool environment.

Water and salt-depletion heat exhaustion and heat cramps should all be treated in the same manner. As previously pointed out, both water and salt-depletion will probably co-exist, so that the specific treatment of the one disorder could make the other disorder manifest clinically. Therefore, assuming that the kidneys can selectively handle either excess water or sodium chloride, salted water should be administered for both water and salt-depletion heat exhaustion. Usually 0.1 to 0.2 percent salt in water given orally suffices. However, if an astronaut is vomiting or seriously depleted, isotonic saline should be given intravenously. Salt tablets of any form are not indicated, for they dissolve too slowly and are very prone to cause gastrointestinal upset. An afflicted astronaut should rest in a comfortable cool environment. Rarely, special cooling measures discussed below might be required.

Both prickly heat and anhidrotic heat exhaustion respond well to continuous exposure to a dry, cool environment. Dry non-irritant clothing must be worn. Washing with an antiseptic soap, such as hexachlorophene,

will help to prevent or control secondary skin infection. If well established, a skin infection might require treatment with a suitable local or systemic broad spectrum antibiotic.

Heatstroke is a medical emergency requiring immediate "heroic" treatment. The body core temperature of an afflicted astronaut must be decreased as quickly as possible to 102° F. An acute lowering of body temperature below 102° F can apparently lead to a cardiac arrhythmias, and should, therefore, be avoided <sup>(32)</sup>. The practicability of various body temperature-lowering methods for use in space should be investigated. Evaporative cooling, accomplished by passing dry air over moist clothing might be possible in the space cabin. More practical, however, might be the use of a space suit liquid cooling garment. In this case, the vasoconstrictive effect of cold, especially on skin vessels, will be an important factor in considering an optimum coolant temperature. It is also noted that the effect of surface cooling is usually markedly enhanced by vigorous skin massage. The administration of cold fluids orally should also be considered for cases which are able to ingest these fluids. At the present time, chlorpromazine is being administered intravenously to patients being cooled for heatstroke, apparently for its role in depressing the hypothalamic center for heat conservation, in promoting peripheral vasodilatation, in abolishing shivering due to cold, and in preventing convulsions, restlessness and other hyperirritable states <sup>(24)</sup>.

For reasons already discussed, an astronaut suffering from heatstroke and associated "shock" should receive oxygen and a vasopressor drug, such as metaraminol, even though such a drug might reduce heat dissipation by producing peripheral vasoconstriction. From the work of Gold <sup>(16)</sup>, administration of a rapid-acting cardiac glycoside intravenously may be valuable in hyperpyrexia or early heatstroke, even in the absence of frank "shock". Such a measure must be undertaken with extreme caution because of the possible presence of marked electrolyte abnormalities which are conducive to digitalis intoxication. Intravenous fluids should be administered with care to avoid precipitation

of acute pulmonary edema, but can be given more intensively if serious salt or water depletion has been evident prior to onset of the heatstroke. The fluid of choice is normal saline. An osmotic diuretic, such as mannitol, might be added to this regimen if the danger of renal damage from "shock" exists. Sedatives or narcotics should not be given in heatstroke. If the astronaut is comatose, attention must be given to maintaining a clear airway, and urethral catheterization.

An astronaut with hyperpyrexia unassociated with other signs or symptoms should rest in a cool environment and be watched carefully. His fluid intake should be kept at an optimum level. A special cooling measure might be indicated if his body core temperature remains elevated or if signs and symptoms of other heat disorders appear.

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## CHAPTER 7

### COLD INJURY AND HYPOTHERMIA

Recent discussions of space suit and spacecraft cabin thermal control have indicated that an astronaut's risk of exposure to an excessive heat loss will be much less than his risk of exposure to an excessive heat load (Chapter 6) during space operations (30, 44, 77). It is even conceivable that potential medical problems from heat loss will be virtually eliminated in future space systems. For the present, however, these problems should be considered possible, especially if an extravehicular astronaut is rendered immobile for a period of time in a shaded space environment. In this situation, local or total body conductive heat loss might be increased by an abnormal amount of moisture in his space suit, by an increased thermal conductivity of his suit insulation due to compression against an external object and by wide-spread contact between his suit and a cold lunar, planetary or spacecraft surface. It is also remotely possible that continued operation of an astronaut's suit thermal control system during such an exposure could be a factor contributing to a medical heat loss problem.

It has been speculated that either artificially-induced hypothermia or more preferably an induction into a state resembling hibernation might provide a means of protecting astronauts from various hazards during long space missions (17, 57). However, the practicability of such a measure remains to be proven.

In this chapter, the pathophysiology, clinical manifestations, diagnosis, prevention, and treatment of cold injury, resulting from excessive local body heat loss, and hypothermia, resulting from excessive accidental total body heat loss, will be discussed briefly. For greater detail than that to be presented here, one can consult the many excellent reviews cited.

#### Cold Injury

##### Pathophysiology

Cold injury is tissue damage which can result from either the non-freezing or freezing of tissues. Since the extent and severity of the damage depends

upon a great number of factors, a critical exposure temperature for cold injury in humans cannot be clearly defined. The major factors which could contribute to this injury in the space situation are the exposure temperature, the duration of exposure and the amount of conductive heat loss contributed by moisture in the space suit or other failures of thermal protection by the suit. Other important factors will be discussed below. To give some idea as to what exposures could cause cold injury, it is noted that past experience, particularly in military operations, has shown that the feet are usually injured following their exposure in excess of 12 hours in water at temperatures below 50°F (immersion foot) or in excess of 24 hours in moisture near freezing (trench foot) (6, 26, 62). Thus cold injury could occur below 10°C (50°F) if the duration of the exposure is sufficiently prolonged (61).

It is important to note that various tissues do not show the same degree of susceptibility to cold injury. Blood vessels, nerves and striated muscles are highly sensitive to cold (6). Skin, fascia, connective tissue, bone and tendon are quite resistant (6). Damage to deep structures, such as nerve and muscle, can therefore occur without the overlying skin being significantly damaged by cold.

The pathophysiology of cold injury remains uncertain (48, 65, 67). One reason for this has been the paucity of tissue from humans available for study during the acute phases of this injury (66). Most authorities believe that cold injury can be secondary to vascular changes in the tissue during cold exposure and rewarming, due to direct injury of the tissue by cold, or from some combination of these mechanisms (6, 8, 16, 26, 51, 52, 62, 63, 67, 89, 92). Because the management of cold injury is directed at these possible mechanisms, they are discussed below in some detail. Although not definitely stated, these considerations apply in particular to cold injury of the limbs. For readily apparent reasons, the damage develops at first distally, then progresses proximally in the limb.

Cold-induced constriction of arterioles and small arteries can conceivably produce local hypoxic tissue damage. Further lowering of the local tissue temperature secondary to vasoconstriction sets up a vicious cycle which leads to further local hypoxia. The vasoconstriction can be not only due to

a normal local response to cold, but also to the centrally-induced, generalized peripheral vasoconstriction which occurs if the total body heat loss is sufficient to force the body to preserve its core temperature (42, 46). Of great interest are the observations that vasoconstriction might not occur if the body does not have to conserve heat, and that constricted vessels in cold extremities can be reopened if the total body heat is maintained at a level bordering on positive heat balance (4, 75, 81, 84). These findings point to the importance of maintaining adequate total body heat during exposure to both local and generalized heat loss.

Apparently to protect the vasoconstricted extremity from cold injury, the so-called hunting or Lewis phenomenon occurs (58). This rather complex response to cold is a periodic vasodilatation which allows periodic surges of warm arterial blood to pass through the cooling tissues (16, 58). It is usually triggered at tissue temperatures below 10°C (50°F) (40, 45). The hunting phenomenon may do little to provide adequate heat and oxygen replacement to cooled peripheral tissues in man, however, for apparently the capillary flow in these tissues increases only slightly while most of the blood passes through arteriovenous anastomoses (39, 45). Moreover, it has also been shown that this phenomenon can be prevented or reduced in magnitude by an excessive total body heat loss (12, 28), or by emotional states such as anxiety (2, 12). Even in subjects who are generally warm, the transient vasoconstriction caused by deep respiration or startle is considerably prolonged when the hand or finger is exposed to cold (7). Therefore the hunting phenomenon might at best be a poor and unpredictable protective mechanism. However, this discussion of the body's attempt to protect itself from cold injury does suggest that specific measures which increase both peripheral blood flow and tissue perfusion might offer some protection from cold injury.

The major vascular mechanism of cold injury appears to be the irreversible vascular occlusion and subsequent tissue hypoxia which follow the re-warming of frozen tissues or tissues exposed to non-freezing cold for long periods of time (6, 26, 51, 52, 53, 68). From observations made in extensive animal experimentation, Kulka (51, 52, 53) described the sequence of cold-induced vascular changes as: arterial and arteriolar con-

striction, excessive venular-capillary dilatation, increased endothelial leakage, erythrostasis, arteriovenous shunting, segmental vascular necrosis and massive thrombosis. He noted that neural, humoral or hemic factors may all contribute to the production of the three basic functional defects of vasoconstriction, venular dilatation and endothelial leakage<sup>(51)</sup>. Mundth<sup>(67, 68)</sup> has also presented evidence which indicates that the primary pathologic process in response to freezing injury appears to be an alteration in the intravascular cellular stability with the formation of platelet and erythrocyte aggregates. It has also been noted that the tissue damage can be enhanced further by vasoconstriction proximal to the injured area, mechanical irritation and bacterial infection<sup>(26, 52)</sup>. As will be discussed, various measures which are directed at improving local tissue perfusion, and inhibiting intravascular cellular aggregation and clotting have had a beneficial effect on tissue survival and function following cold injury.

Although freezing can cause tissue damage by mechanically disrupting cellular structure, especially in highly specialized tissues, it is a well known fact that certain tissues can survive unquestionable freezing<sup>(52, 63)</sup>. On the other hand, death of other tissues has occurred in spite of there being no histological evidence of disruption<sup>(62)</sup>. The reason for this has been postulated in reviews by Meryman<sup>(61, 62, 63)</sup>. He stated that during freezing, intracellular dehydration occurs. This dehydration results from extracellular ice crystal formation. The remaining, unfrozen extracellular fluid is rendered hyperosmotic with respect to the intracellular fluid, so that water is drawn osmotically from the cells. The high concentrations of electrolytes and other cell constituents then causes cumulative injury to the cell through biochemical means, such as denaturation from electrolyte concentration and unnatural chemical bonding<sup>(63)</sup>. Meryman also noted that rapid freezing is tolerated better than slow freezing<sup>(61, 62)</sup>. However, he quoted reports indicating that the successful survival of rapidly frozen tissues depends primarily on rates of freezing and subsequent rewarming which cannot be attained in the clinical situation.

It is possible that a prolonged exposure of certain tissues to low non-freezing temperatures could cause an irreversible imbalance in the function

of metabolic enzyme systems (48, 77). However, this view is not definitely stated by other authors (6, 26, 89).

Outside of the conclusion that cold or frozen tissue should be rewarmed as quickly as possible, no specific beneficial measures appear to be indicated by the above considerations of the mechanisms of direct injury by cold. Therefore the prognosis apparently cannot be improved if the damage has been caused by the direct effect of cold. Notably, this contrasts to the significant improvement derived from measures which are directed at the vascular mechanisms of cold injury.

### Clinical Manifestations

Cold injury usually occurs quite insidiously, so that warning symptoms are often insufficient to prevent tissue damage. The only warning symptoms may be paresthesias followed by anesthesia of the exposed part. In cases of hand exposure, manual dexterity will, of course, be impaired. The skin is usually erythematous at first, but then becomes pale or waxy-white in appearance. Frozen tissue is described as "dead white". It is hard and may even be brittle. It is completely lacking in sensation and movement.

In the past, cold injury has been classified clinically under one of four categories — chilblains, immersion foot, trench foot, and frostbite. Although this more operational classification could apply to cold injuries in space, it is generally believed that such injuries are best classified simply as two types — freezing or non-freezing. Even this classification could be considered inappropriate, for a local cold exposure in space would undoubtedly produce a graded injury, characterized by a possible freezing injury of the most exposed part and lesser degrees of non-freezing injury progressing centrally from this part. Fortunately, however, tissue damage and its management are very similar for both freezing and non-freezing injury, the only variable being severity of the damage.

Most authors describe cold injuries as falling into one of four degrees of severity. Since it takes several days for the degree of freezing and non-freezing tissue damage to become fully manifest, this classification is of little value from therapeutic and prognostic standpoints in the immediate

period after a cold exposure (6, 26, 48, 65). Mills has pointed out that a cold injury in its early stages may be classified often as no more than superficial or deep (64). However, the broader classification summarized below from many authors (6, 11, 20, 26, 48, 70, 74, 92), is useful for a detailed description of the clinical manifestations and the course of cold injury as related to its severity.

First Degree - hyperemia and edema. During rewarming, the skin initially becomes mottled and cyanotic, then red, hot, and dry. This hyperemia blanches poorly on pressure, with capillary refilling being very sluggish or absent. At first there is frequently an intense burning or itching sensation; later there is a deep-seated ache. In milder cases, these symptoms may cause intense discomfort for several hours, and then gradually disappear without serious sequelae. In more severe cases, they are not only more severe and prolonged, lasting for periods up to several days, but deep aching pain, paresthesias, cyanosis, hyperhidrosis and coldness of the injured part may appear 2 to 3 weeks after injury and persist for many months. Edema usually begins within 3 hours after rewarming and usually disappears within 10 days if the patient is at rest. Desquamation of the superficial layers of the skin begins 5 to 10 days and may continue for several weeks.

Second Degree - vesicle formation. The signs and symptoms of first degree cold injury are also present. However, the edema is usually not marked and disappears within 3 to 5 days after rewarming. Light touch and position sense are usually absent. A throbbing or aching pain is usually experienced from 3 to 20 days after injury. Blisters and, in more severe cases, huge blebs may appear within 6 to 12 hours after rewarming. These vesicles, which usually form on the dorsum of the fingers, hand and great toes, and on the heel, are often deep in the epidermis. However, they do remain superficial to the germinative layer, so that the epidermis is regenerated. The vesicles may contain blood as well as fluid transudate. They dry, forming black eschars within 10 to 24 days after rewarming. Hyperhidrosis may occur as well at this time. The eschar gradually separates, leaving a thin, soft, poorly keratinized skin which is easily traumatized.

Third Degree - necrosis of the skin and subcutaneous tissue. This cold injury involves the full thickness of the skin and often extends into the subcutaneous tissue. Vesicles may appear at the periphery of the area of third degree injury. Edema of the involved part is extensive,

usually disappearing with 6 days. This injury is associated with burning, aching, throbbing or shooting pains which begin in the second week and persist for about 5 weeks. The skin over the area of a third degree injury usually dries to a black, hard eschar, which eventually separates from poorly vascularized underlying granulation tissue. Epithelialization of this area is gradual, healing often taking 2 to 3 months. Hyperhidrosis and cyanosis of the involved part may appear between the fourth and tenth week after injury and persist for months, resulting in a prolonged uncomfortable convalescence. It should be noted that trauma due either to injury other than cold or to superimposed infection may complicate this degree of cold injury and result in a more extensive tissue loss.

Fourth Degree - destruction of the entire injured part, including bone, with resulting loss of the part. Upon rewarming, the skin becomes mottled and cyanotic. Edema begins rapidly, starting within an hour and reaching a maximum within 6 to 12 hours. Bleb formation is common. In most fourth degree cold injuries, the extent of injury becomes apparent only as the edema resolves, the eschar formation or gangrene frequently not being evident until 2 to 3 weeks after injury. In severe injuries, the affected tissue will progress rapidly to dry gangrene and mummification. Demarkation between living and dead tissue becomes fully apparent in about one month, and extends down to bone in 2 months or more after injury.

Finally it should be noted that following any degree of cold injury, an astronaut could become sensitized to some degree to a further cold (65, 66). With a mild injury, the involved part might be sensitized to cold for days or weeks and with a severe injury, this sensitization might be permanent (26). For such cases, even a minor exposure to cold may be followed by an exaggerated and prolonged reactive vasodilatation with associated redness, edema and tingling pain. Edema of a urticarial type and even systemic reactions are also possible (91).

### Diagnosis

The diagnosis of cold injury in space should be obvious on clinical observation, with no special diagnostic procedures being required. It is again pointed out that cold injury often requires several days to become fully manifest, so that an early prediction of the extent and severity of a cold

injury will be impossible.

### Prevention

Emphasis is placed on the importance of recognizing and adequately correcting for certain physiological and space suit and spacecraft cabin design factors which will undoubtedly influence the risk of exposure of the astronaut to an excessive heat loss and subsequent cold injury during space missions. As mentioned previously, these factors would apply particularly to operations in the space suit in a shaded space environment.

The distal parts of an astronaut's extremities, especially the fingers, will be highly susceptible to cold injury, due not only to their large surface area per volume of tissue and their usual marked vasoconstrictive response to cold, but also the fact that, for mobility, only minimal suit insulative material will surround these parts. Moisture in the suit and direct contact of the surface of the suit with other materials in a shaded space environment could lead to an excessive conductive heat loss, particularly from a minimally insulated distal extremity. When designing and fitting space suits, consideration must be given to avoiding constrictions and tightness which in any way might jeopardize the blood flow to an extremity, and thus increase the susceptibility of the extremity to cold injury. The "coolant" of suit liquid cooling systems could pass through hand and foot areas last, so providing a "fail safe" effect.

As mentioned previously, the maintenance of adequate total body heat during a localized or extensive heat loss from the space suit might serve to protect an astronaut from cold injury by preventing the localized vasoconstriction or the centrally-induced, generalized peripheral vasoconstriction in response to cold. Thus if an astronaut is subjected to an excessive heat loss through one or more areas of his suit, he might attain some protection from cold injury by having the amount of heat removed from his suit by the life support system reduced, even to the point of allowing him to go into slightly positive heat balance. Increased body heat production through physical activity would play a similar role. However, it must be remembered that anxiety and other possible factors (e. g., hypocapnia) might tend to prevent this protective effect <sup>(75)</sup>.



The importance of continuous physical activity for providing sufficient metabolic heat to maintain thermal balance in the space suit under all circumstances is readily apparent. The suggestion that ingestion of food of a high specific dynamic action prior to a possible exposure to an excessive heat loss might have some protective value, by reason of its tendency to increase the basal heat production of the body, has not been supported in recent experiments (49, 75).

It has been suggested that agents which prevent or abolish a cold-induced vasoconstriction might be useful in protecting an exposed part from cold injury (75). However, no topical vasodilators appear to exist which can be used to give a graded response, or which will not be absorbed and hence result in a whole-body effect. Systemic administration of such agents will probably always be contraindicated unless their action is highly specific and the cold exposure anticipated will be of a short duration.

The marked influence of systemic hypoxia on the extent and severity of tissue damage by cold is well known (20, 55). In space, this hypoxia would be most likely caused by a reduction of the ambient oxygen tension. On the other hand, an elevated partial pressure of oxygen tends to produce a peripheral vasoconstriction which can contribute to cold injury (29). It is apparent, therefore, that the vascular effects of oxygen at the partial pressures to be used in the space suit should be investigated.

The view is generally held that prolonged exposure to weightlessness will produce both a decrease in the total blood volume and a decrease in capacity of the vessels in the lower extremities to maintain their tone when an astronaut stands upright in a gravity environment. If these effects are not prevented or corrected before an astronaut walks on a lunar or planetary surface, a potential or manifest state of orthostatic hypotension might result, depending on the ability of his body to compensate for his inadequate circulating blood volume. This compensation would occur mainly by peripheral vasoconstriction, which could lead to the astronaut being more susceptible to cold injury of the feet. It also considered possible that this susceptibility might be enhanced by the use of elastic garments to prevent orthostasis.

All environmental conditions being equal, the Negro appears to be about six times more vulnerable to cold injury than the Caucasian (26). It appears

that a physiologic basis does exist for this difference (60, 76). As well, the geographic origin of man seems to be a significant factor among Caucasian personnel in the incidence of cold injury, for origin from the warmer climates of the United States has been shown to predispose to cold injury (16, 66, 70). However, whether these factors would be significant enough to influence selection of astronauts is debatable. Finally, it will be necessary to rule out the presence of cold agglutinins in astronaut candidates.

It is pointed out again that following any degree of cold injury, an astronaut could become sensitized to some degree to cold. With milder injuries, the involved part might be sensitized to cold for days or weeks, and with more severe injuries, this sensitization might be permanent.

As will be discussed under "hypothermia", the possible protective effect of cold acclimatization, even if it exists, remains debatable.

#### Treatment

The treatment of cold injury remains controversial, due mainly to the lack of knowledge of the mechanisms of cold injury (6, 55, 65, 70). Since more definitive forms of therapy will not be accomplished in the space environment, the more conservative methods for the treatment of cold injuries in space will have to suffice. It is noted that all cold injuries receive basically the same treatment from the beginning, modifications being carried out as indicated by the degree of injury.

Initially, the injured part should be completely uncovered and all items of clothing or equipment which might in any way restrict blood flow to the part removed. Rewarming of the cold-injured part to body temperature should be accomplished as quickly as possible by exposing the part to temperatures recommended above 32°C (89.6°F) but not above 42°C (107.6°F) by most authors (6, 16, 33, 34, 55, 65, 72). Methods which maximize heat transfer by conduction are preferred. Even though a water bath will not be practical in space, surrounding the injured part with flexible plastic containers, such as a balloon splint, containing warm fluid might be a useful substitute. Moist warm towels might also be used. It is pointed out that good conductive heat transfer can be obtained by placing the injury in contact with warm areas, such as the axilla, perineal area, and trunk, of either an

injured or uninjured astronaut's body. As will be discussed, rewarming of an astronaut suffering from generalized hypothermia should be done gradually, so that the above methods of rewarming will apply only to cold injured areas. Massage of the rewarming part is contraindicated because of the possibility of causing further trauma to the injured tissue (34, 65, 70, 89). The use of ultrasound to rewarm cold-injured tissues is not recommended, as there is evidence of it having deleterious effects in deep tissue injuries (65).

The major aims of treatment after rewarming should be the prevention of further trauma to and possible infection of damaged tissues, and the maintenance of an optimum range of movement in the damaged part (19, 55). It is again emphasized that the degree and extent of cold injury may become fully evident only after several days. Hence a more serious injury than that observed initially should always be anticipated.

The damaged part should be gently washed with a mild, antiseptic soap (e.g., hexachlorophene soap) (65). Whereas lesions without vesicles are usually left exposed under sterile conditions on Earth, all cold injuries in space should be dressed in order to provide optimum protection from further trauma and infectious organisms. Dressings should be loose and dry, and cotton pledgets should be placed between digits to avoid maceration (50, 65). Debridement of vesicles should not be undertaken initially unless they are disrupted (6, 26, 33, 54, 89). Petrolatum dressings as indicated in burn therapy should never be applied (6, 65, 92).

Antibiotics are usually given to cases of cold injury only if there is obvious deep infection (55, 65, 70). However, in the space situation, consideration might be given to prophylactic antibiotic administration, especially to possible third and fourth degree cold injuries, in order to maximize the protection of the damaged tissue from invasion by pathogenic organisms. Such therapy should be continued until a clean demarkation is evident.

Dressings should be changed daily. At this time, wet dead tissue from ruptured vesicles might be removed, infected vesicles opened and, if indicated, constricting eschars bivalved (6, 33). Optimum cleanliness must be maintained. If in any way contaminated, the injured area should be gently washed with antiseptic soap and dried. As soon as the acute in-

flammation has subsided, active physiotherapy should be commenced (6, 55, 92). The performance of digital exercises of each joint of every involved digit throughout the waking hours and Buerger's exercises at least four times daily have been recommended (65). It should be kept in mind that all parts of an injured extremity should be exercised.

All eschars should be allowed to separate rather than being removed surgically (55). In fourth degree injuries, so-called physiological amputation will occur, usually in 2 months or more after injury. If adequate care is taken to keep the injured part dry and free from infection, the possibility of wet gangrene and the requirement for surgical amputation will be remote. Circumferential eschars, which tend to constrict and so restrict blood supply, should be bivalved if possible (6, 33, 55).

Although pain is usually not a serious problem in cold injury, a non-narcotic analgesic or tranquilizing drug might be indicated in the period after thawing (6, 48, 65). A tetanus toxoid booster prior to missions in space should eliminate the need for such an injection following cold injury. A cold-injured astronaut should receive a vitamin supplemented diet which is high in calories and protein content.

Various measures directed at improving local tissue perfusion and inhibiting intravascular cellular aggregation and clotting have been studied for their possible beneficial effect on tissue survival and function following cold injury. Meryman pointed out that it would not be fair to presume that none of these measures have been clinically successful, since the evaluation of therapeutic procedures in clinical frostbite is hampered by the lack of criteria for determining the severity of injury prior to the initiation of therapy. However, the vasodilator drugs have generally not been proven effective either experimentally or clinically (6, 26). This might in part be due either to a negation of the possible increase in blood flow through the dilated vessels at the site of injury by the systemic hypotension associated with use of these drugs, or to delays in attempting to forestall circulatory obstruction immediately after thawing before such obstruction develops.

Regional sympathectomy has been somewhat successful in animal experi-

ments, reducing both edema and the amount of tissue loss (25, 37). As a therapeutic measure in human cases, it has been highly effective in reducing the number and severity of sequelae, such as coolness, hyperhidrosis, pallor, vasospastic complaints, and ulcers, which follow cold injury (78, 79). The inherent difficulties in assessing the effectiveness of sympathectomy on the extent of tissue loss in human cases are readily apparent. Surgical sympathectomy is a highly specialized, major procedure, the performance of which would be precluded by the space situation. However, success in the treatment of sequelae of cold injury by sympathectomy would suggest that the sympatholytic drugs and, in certain cases, regional sympathetic nerve block with a local anesthetic might also be effective in the treatment of these sequelae.

Low molecular-weight dextran has been administered to cold injury cases because it has been shown to be a specific agent for the inhibition of intravascular cellular aggregation and the improvement of small vessel blood flow in injured tissue (67). The beneficial results obtained with this agent in animal experiments do not appear to be attributable to the expansion of plasma volume and hemodilution which it also produces (5, 67, 68, 69). The actual clinical effectiveness of this drug remains to be established, however (26, 33, 69, 71, 80).

Heparin, used to prevent microvascular clotting, has had success in animal experiments (33, 73). However, its effectiveness in human cold injury cases has not been proven (6, 55, 92).

If vasodilating, anti-sludging, or anti-coagulant agents are in fact proven clinically useful, in the treatment of cold injury, it is readily apparent that they must be administered as soon as possible after and perhaps before starting the rewarming of the injured area, and for many hours to several days thereafter. Unfortunately, the early administration of such agents to cold injury cases has up to this time been difficult and most often impossible to accomplish. Therefore the results of well controlled animal experiments may well have to be relied on in anticipating their clinical effectiveness for some time to come.

Steroids, administered in attempts to limit the inflammation associated with cold injury, and flavonoids, taken for the reduction of capillary perme-

ability and fragility in cold injured tissue have not been beneficial in the treatment of cold injury <sup>(90)</sup>.

## Hypothermia

### Pathophysiology and Clinical Manifestations

Hypothermia, which has been discussed in several excellent reviews, has been defined as a state of body temperature which is below normal in a homeothermic organism (9, 13, 18, 27, 54, 56, 82, 83, 85). Little (59) attempted to make this definition more meaningful by stating terms which could be used to characterize the depth and duration of the hypothermia under consideration. The depth of hypothermia was categorized in terms of body core temperature, as light ( $37^{\circ}$  to  $32^{\circ}\text{C}$ ; or  $98.6^{\circ}$  to  $89.6^{\circ}\text{F}$ ), intermediate or moderate ( $32^{\circ}$  to  $26^{\circ}\text{C}$ ; or  $89.6^{\circ}$  to  $78.8^{\circ}\text{F}$ ), deep ( $26^{\circ}$  to  $20^{\circ}\text{C}$ ; or  $78.8^{\circ}$  to  $68^{\circ}\text{F}$ ), and profound (under  $20^{\circ}\text{C}$ , or  $68^{\circ}\text{F}$ ); and the duration of hypothermia as acute (few hours), and chronic or prolonged (many hours, days, or weeks). This classification has a greater application to considerations of hypothermia used as a therapeutic tool than to considerations of hypothermia acquired accidentally. However, each depth of hypothermia categorized above appears to correlate well with the clinical picture an astronaut might present if rendered hypothermic to a particular level of body core temperature. The clinical features of these various depths of hypothermia are:

**Initial Response to Cold.** The initial response to cold mimics intense stimulation of the sympathetic nervous system, being characterized by intense shivering, marked peripheral vasoconstriction, elevation of systemic arterial pressure and significant increases in oxygen consumption, respiratory rate, and cardiac output (59). This stress response may actually produce a slight rise in temperature, and so delay the onset of hypothermia which will eventually result if physiological compensatory mechanisms are inadequate (9).

**Light Hypothermia** ( $37^{\circ}$  to  $32^{\circ}\text{C}$ ; or  $98.6^{\circ}$  to  $89.6^{\circ}\text{F}$ ).

This depth of hypothermia is characterized by a sensation of severe cold and intense shivering which may be painful, especially around the neck. The toes and fingers become increasingly painful, then numb. Respiration is increased in rate and depth from the onset of hypothermia but subsequently decreases, especially below  $34.5^{\circ}\text{C}$  ( $94.1^{\circ}\text{F}$ ), in a manner that can lead to respiratory acidosis

in spite of an overall normal arteriovenous oxygen difference being maintained (83, 87). It is also pointed out that as the body temperature decreases, the solubility of carbon dioxide in body fluids increases and the oxygen carrying capacity of the blood decreases. An increase in metabolic rate occurs during a normal response to cold, persisting until the core temperature has fallen to approximately 35°C (95°F), and thereafter declines to reach basal values or lower in the intermediate or moderate hypothermia range (15, 27). As the temperature falls, the heart rate decreases. During this period, the blood pressure falls, but only gradually (15).

Intermediate or Moderate Hypothermia (32° to 26°C; or 89.6° to 78.8°F). At this depth of hypothermia, the individual becomes increasingly somnolent and resistant to pain, and finally loses consciousness (3, 32). Shivering ceases between 33°C (91.4°F) and 30°C (86°F), but muscular rigidity may persist to 27°C (80.6°F) (15). Respiration will continue to decrease, becoming irregular about 30°C (86°F) and finally cease about 28°C (82.4°F) (15). Cardiac arrhythmias (nodal rhythm, auricular fibrillation, ventricular extrasystoles, etc.) appear at core temperatures below 30°C (86°F) (15). Ventricular fibrillation becomes an increasing hazard at temperatures below 28°C (82.4°F) (87). Hypothermia in this range might occasionally aggravate epilepsy and certain other types of seizures (59).

Deep Hypothermia (26° to 20°C; or 78.8° to 68°F). Death usually occurs about 25°C (77°F), from either ventricular fibrillation or cardiac asystole (3, 15). However, the lethal temperature might be quite variable as demonstrated by a case in which a woman survived a fall in core temperature to 18°C (64.4°F) or even lower (15, 57).

Profound Hypothermia (under 20°C; or 68°F). Survival of accidental hypothermia to this level is considered highly unlikely.

The general effect of hypothermia is currently thought to be entirely depressive, even though there is an increasing tendency of the heart to become more sensitive to the development of arrhythmias and the central nervous system to become more excitable as the core temperature of the body falls. Accordingly, the slowdown of body functions do not appear to parallel each other. Hence a potentially dangerous physiochemical state can result (57). The physiologic changes that occur in response to hypothermia are

complex and not well understood. Yet they may be tolerated for some period of time without harm. For example, Talbott<sup>(85, 86)</sup> and Dill and Forbes<sup>(27)</sup> treated patients suffering from psychoses by slowly cooling them to a rectal temperature of about 26.5°C (79.7°F). The patients were maintained at this temperature level for periods of up to 24 hours and then slowly rewarmed. There were two deaths from cardiac failure during the hypothermic phase in the series of 20 cases, with no after-effects being noted in the survivors.

The most serious complication of hypothermia has been ventricular fibrillation, which occurs particularly at temperatures below 28°C (82.4°F). Unfortunately, there appears to be no proven method of reversing this arrhythmia in an individual who is in the hypothermic state. Moreover, it is highly unlikely that the standard methods of defibrillation, which are in themselves often only momentarily effective, could be undertaken in the space situation.

Lewis<sup>(54)</sup> has cited work which has shown that an impressive irreversible cardiac failure can develop in cases of prolonged hypothermia. This fatal event appeared particularly during rewarming. Conflicting evidence has been presented on the important question of the occurrence of other hypothermic organ damage<sup>(59)</sup>.

The most common complication which might occur on rewarming a hypothermic astronaut is so-called rewarming shock<sup>(31)</sup>. This syndrome consists of the development of hypotension and acute circulatory collapse, which is characterized by tachycardia, diminished cardiac output and inadequate respiration<sup>(12)</sup>. It appears to be due to acidosis which is predominantly metabolic in origin although, as previously mentioned, carbon dioxide accumulation due to cold-induced respiratory depression and increased solubility of this gas in cooled body fluids also occurs and might contribute to some degree to the acidosis<sup>(59)</sup>. Shivering and rapid warmth-induced increases of blood flow through the vascular beds of cold muscle masses during rewarming can result in marked increases of circulating acid metabolites, and so produce or aggravate rewarming shock. Undoubtedly other factors can also be implicated in the etiology of rewarming shock. A



marked warmth-induced peripheral vasodilatation might itself be conducive to shock or seriously aggravate the tendency to shock produced by metabolic acidosis. As well, the loss of circulating plasma volume, which occurs during prolonged hypothermia, might be inadequately restored if rewarming is accomplished rapidly (15, 85, 86, 88). There is also the possibility that cardiac inadequacy, caused by a reduction of muscular glycogen or myocardial damage from prolonged hypothermia, might contribute to rewarming shock (15).

Another significant complication of rewarming has been discussed by Burton and Edholm (15). It has been noted that rapid increases in blood flow through cooled parts of the body can result in a large volume of cooled venous blood returning to the heart. For example, Behnke and Yaglou (10) recorded sharp falls of gastric, oral and rectal temperatures initially on rewarming their subjects. Burton and Edholm (15) thus suggested that the resulting drop in cardiac temperature might produce cardiac arrest or ventricular fibrillation, particularly under conditions of rapid rewarming.

### Diagnosis

The level of the core temperature of a hypothermic astronaut should be determined as soon as possible in order to decide on the potential seriousness of the situation and thus the therapeutic approach to be followed. For example, shivering can occur over a wide range of temperatures (37° to 30°C; or 98.6° to 89.6°F), so as a clinical finding it alone could indicate either a mild response to cold or a serious clinical situation. On the other hand, an astronaut could be stuporous or unconscious, not shivering, and yet hypothermic (core temperature less than 30°C, or 89.6°F). The level of core temperature might conceivably also be necessary to establish the diagnosis of hypothermia as distinct from other causes of stupor or unconsciousness. If ever possible in space, determination of blood pH could serve as a valuable adjunct in deciding on specific therapy of a hypothermic astronaut.

### Prevention

The question arises as to whether or not acclimatization of man to a cold

environment is possible and if so, whether or not such a long-lasting adjustment of physiological functions should be induced in an astronaut if unusually high risks of excessive local or total body heat losses are anticipated during operations in space. Although it has been well established that true physiologic acclimatization to heat occurs (Chapter 6), Davis <sup>(21)</sup> has pointed out that there is a significant group of investigators who have found that there is no defined evidence of cold acclimatization in man. On the other hand, various recorded changes in the reaction of the peripheral blood circulation to cold and in the cold-induced increase in metabolism after repeated or prolonged cold exposure have been interpreted as evidence of acclimatization to cold in man.

In his excellent review and from his studies in this area, Hellström <sup>(46)</sup> pointed out that much evidence can be accumulated to show that cold-induced vasodilatation is more marked and comes on more rapidly in individuals who are chronically exposed to cold in their occupations, as compared to those who work in a warm environment. These workers also demonstrated a higher pain threshold and better manual functioning on cold exposure, and a lowered response to the cold pressor test as compared to those who work in a warm environment. He found no convincing evidence of a seasonal variation in these parameters studied in students. Daily exposure of one hand to cold water (temperature initially 3°C, rising to 12°C during 30 minutes) for 11 to 15 consecutive working days in the early summer in a thermally "neutral" environment did not appear to alter hand blood circulation or the deteriorating effect of cold on hand function. Such was also the case when the same local cold exposure was applied 6 days a week for 3 weeks during the winter to individuals who sat naked at 15.5°C ambient air temperature for 70 minutes. However, a reduction of cold-induced pain in the exposed hand and a decrease in the cold pressor response took place in both experiments.

Davis <sup>(21, 22, 23, 24)</sup> has managed to produce a significant elevation of the shivering threshold of individuals exposed, nude, 8 hours a day for 31 days to an ambient air temperature of 11.8°C. This was also found to result from seasonal or climatic temperature decreases. He concluded that the elevation of the shivering threshold appears to define the occurrence

of cold acclimatization in man with some precision. Using this criterion, Davis demonstrated that the seasonal cold acclimatization in man was not retained over the summer whereas the acclimatization following the chronic nude cold exposure was retained through at least one summer season. Heat acclimatization in these studies did not affect artificially or naturally induced cold acclimatization. This finding, in the light of the demonstration by others that heat acclimatization is unaffected per se by cold exposure, indicates both acclimatizations can co-exist in an individual (36, 47, 83). Studying other parameters, Davis found that the initial cold-induced heat production in unacclimatized subjects was consistently higher (value of 64 percent above basal) in those studied in the summer as compared to those studied in the winter season (value of 30 to 40 percent above basal). After the chronic nude cold exposure, this response stabilized around 30 to 40 percent in both groups. Lastly, he found that the body core temperature of the chronic exposure group decreased significantly on cold exposure.

Numerous other studies described in the literature point as well to the fact that most past work on acclimatization to cold in man has been concentrated on efforts to establish criteria for it, prove its very existence in various groups of cold-exposed subjects and evaluate the degree of cold exposure necessary to produce changes of physiological reactions which deserve interpretation as evidence of acclimatization to cold. It is apparent that the possible degree of cold acclimatization which can take place in man has not been startling -- a sharp contrast to the rather overwhelming evidence that true physiologic acclimatization to cold exists in other non-hibernating homeotherms<sup>(43)</sup>. Moreover, it does not appear to have been proven that cold acclimatization can actually offer man significant protection from cold injury or accidental hypothermia. Thus, at the present time the conclusion can be drawn that even if cold acclimatization could confer some protection in an astronaut, the practicability of inducing it might be outweighed by the exposure temperature and duration which would be required for its induction. As well, possible loss of cold acclimatization over early months of a prolonged mission in space would also

suggest impracticability.

### Treatment

In order to minimize the risk of the complications of hypothermia discussed previously, an astronaut's normal body temperature should be restored as slowly as possible. By allowing the peripheral tissues to rewarm slowly, the acid metabolites and carbon dioxide which have accumulated in these tissues will be slowly washed out into the systemic circulation. Thus adequate time will be allowed for the breakdown and buffering of these metabolites, so preventing severe metabolic acidosis and possible rewarming shock. Moreover, a marked warmth-induced peripheral vasodilatation might itself be conducive to shock or seriously aggravate the tendency to shock produced by metabolic acidosis. It is also possible for the volume of plasma lost during a prolonged period of hypothermia to be inadequately restored if rewarming is accomplished rapidly <sup>(15)</sup>. Lastly, slow rewarming decreases the risk of a further drop in cardiac temperature, and so possible fatal cardiac arrhythmias, by keeping the flow of cold venous blood from the cold peripheral tissues to the heart to a minimum.

To accomplish slow rewarming, the entire body surface of a hypothermic astronaut should be exposed to normal environmental temperatures (about 23°C; or 72°F). Accordingly, his body will be allowed to rewarm by metabolic activity alone. As noted elsewhere in this chapter, a local cold injury should, however, be rewarmed as quickly as possible. Under certain circumstances, a hypothermic astronaut might have to be rewarmed while in a space suit. Optimum temperature control settings which will allow a slow rewarming of his body will have to be determined, depending on whether a gas or fluid system is used for temperature control in the suit.

Whether a drug such as chlorpromazine should be administered to minimize shivering during the rewarming process remains controversial <sup>(69)</sup>. This measure could keep the acid metabolites contributed by muscular activity to a minimum, so reducing the tendency to rewarming shock due to metabolic acidosis. As well, the metabolic heat output by muscular activity could be minimized, so allowing a slow rewarming of the body. However,

since drugs such as chlorpromazine are also vasodilatory, their use might be contraindicated.

If rewarming "shock" occurs, intensive treatment of this serious event should be commenced immediately, with appropriate measures being selected as sound clinical judgment dictates. A solution of glucose, saline, and bicarbonate in water should be administered intravenously. Oxygen should be given. An appropriate vasopressor, such as metaraminol, might be indicated. If the possibility of cardiac damage from the hypothermia exists, a cardiac glycoside, such as digoxin, might be given intravenously. Possible external sources producing excessive body heating should be removed.

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## CHAPTER 8

# MEDICAL PROBLEMS DUE TO PARTICLE AND DROPLET CONTAMINATION OF THE SPACECRAFT CABIN ATMOSPHERE

### Introduction

Particles and droplets of all sizes tend to remain suspended in the weightless environment. Various forms of particulate and liquid matter can, therefore, present much greater hazards if introduced into a confined atmosphere in space than if introduced into a confined atmosphere on Earth. These contaminants might not only give rise to certain medical problems in space, but also might produce temporary or permanent malfunctioning of spacecraft components which are vital to the safety of the mission.

By recognizing all possible sources of particles and droplets which might contaminate the spacecraft cabin atmosphere, various preventive and control measures can be taken to eliminate or minimize both potential and real particle and droplet hazards in space. As well, an astronaut might take specific measures to protect himself in a "high risk" situation. However, even though these measures might seemingly eliminate the likelihood of medical problems in space from contaminant-astronaut contact, it still must be assumed that such problems might be the result of an unforeseen accident or failure of the environmental control system to remove rapidly enough larger particles and droplets of debris which will inevitably be introduced into the spacecraft cabin atmosphere. Therefore the various clinical problems which might arise if the astronaut should be exposed to particle and droplet contamination of the spacecraft cabin atmosphere should be predicted and their management in space considered.

### Sources

A simple classification of the major possible sources of particle and droplet contamination of the spacecraft cabin atmosphere is presented in Table 8.1. These sources fall under one of two categories - exogenous

sources, or sources existing outside of the spacecraft in space, and endogenous sources, or sources existing within the spacecraft itself.

EXOGENOUS

Meteoroid  
Extravehicular

ENDOGENOUS

Construction  
Maintenance and Repair  
Preflight  
Inflight  
Operation  
Food - Water - Waste  
Astronaut  
Experiment

Table 8.1 Sources of Particle and Droplet Contamination

The major exogenous sources are meteoroids and other extravehicular sources. Meteoroids which completely penetrate the wall of the spacecraft will lead to free-floating particles of meteoroid and wall. Further particle and even droplet contamination can result if structures within the cabin are disrupted by fragments of meteoroid and wall or by the blast wave produced by the "explosive oxidation" of vaporized meteoroid and wall materials. Fumes and smoke can be produced by the "explosive oxidation" and possibly by fires caused by the ignition of combustible materials by molten and hot fragments of meteoroid and wall. Fragments may also disrupt electrical circuits and structures which contain flammable liquids and gases to produce fires. A meteoroid which does not completely penetrate the spacecraft wall might still result in particle contamination of the spacecraft cabin atmosphere by producing fragmentation, or spallation of the inner surface of the cabin wall.

Other extravehicular sources, primarily of particle contamination, are

extraterrestrial dust and possibly particles of organic matter. Such particles could adhere to the space suit or to other equipment during extravehicular operations on lunar or planetary surfaces. Samples taken from extraterrestrial environments are also potentially contaminating, especially if they are in the form of small particles or in a liquid state, and are to be analysed on board the spacecraft.

It is thought that almost all particles and droplets which can contaminate the spacecraft cabin atmosphere will originate from endogenous sources, or sources existing within the spacecraft cabin itself. Metal particles and dust may remain within the spacecraft following its construction and subsequent checkout. During preflight and inflight maintenance procedures, it might be possible, for example, to release non-chemical particles such as metal, glass, and plastic through breakage, chipping, or dislodgement; to release chemical particles such as lithium hydroxide or superoxides from the environmental control system, or chemical droplets from biochemical or other analytical systems; and to release microbiologically-contaminated water from the waste disposal system. Also during the normal operation of the spacecraft, particles and droplets might be introduced into the spacecraft cabin atmosphere through dislodgement, chipping, and breakage.

Food, water, and waste sources of particle and droplet contamination are apparent. It is noted that solid foods which tend to crumble when handled could be a likely source of particle contamination.

An astronaut could well be the greatest source of particle and droplet contamination of the spacecraft cabin atmosphere. Hair and desquamated epithelium, especially as "dandruff", is shed continuously from the body surface. Talking, coughing, and sneezing will eject droplets of saliva and respiratory tract mucus into the atmosphere. Lint can be released from the astronaut's clothing, Velcro fasteners, and towels. Droplets of urine and wash water, and fecal particles might be accidentally released into the atmosphere. Vomiting will be an extremely serious potential contamination hazard.

Finally, it should be noted that in-space experiments which utilize



chemicals, or fragmentable materials or apparatus might create significant potential particle and droplet hazards, especially if chemicals in biochemical or other analytical systems are to be replaced or if such systems are to be serviced in space.

#### Preventive, Control and Protective Measures

A number of obvious preventive, control and protective measures may be taken to eliminate or minimize potential or existing particle and droplet hazards in space. Various preventive measures are: the selection and design of systems which present minimum potential particle and droplet hazards, especially if serviced in space; the exclusion or shielding of potentially contaminating systems and subsystems from the rest of the spacecraft cabin environment; the use of materials which are non-combustible, lint-free, and do not splinter, flake or shatter; the preparation of foods which do not crumble or powder; the use of contamination "proofed and proven" devices for shaving, haircutting, teethcleaning, washing, urination and defecation; the use of "paper strip" techniques whenever possible for biochemical analyses; and the removal of all metal and other particles created during the manufacture and servicing of the spacecraft before flight. Some control measures are: the compartmentalization of the spacecraft interior, thus separating or being able to separate living, and various "high risk" areas from each other; the provision of a regulatable, efficient air ventilating-filtering system and "vacuum cleaners" which can reach anywhere in the spacecraft; the capability of venting a contaminated compartment in space; and procedures for "decontaminating" astronauts and equipment after extravehicular operations on lunar and planetary surfaces. Various protective measures are: the placing of suitable protective equipment such as masks, eye shields, and total body garments throughout the spacecraft, readily available for use; the wearing of protective equipment in a "high risk" situation; keeping the number of astronauts exposed to a "high risk" situation, such as while servicing the environmental control system, to a minimum; and the placing of adequate shielding around instru-

ments which can be affected by particle and droplet contaminants.

### Predicted Medical Problems

The medical problems which can result if suspended particles or droplets come into contact with an astronaut will be determined by their physical, chemical, and microbiological properties. Taking into consideration the properties which the various possible particle and droplet contaminants of the spacecraft cabin atmosphere might have, the major medical problem areas appear to be; eye problems due to non-chemical particles\* and chemical particles and droplets; skin burns due to chemical particles and droplets; and medical problems due to the inhalation of non-chemical, chemical, and microbiologically-contaminated particles, and chemical, and microbiologically-contaminated droplets. A brief discussion of various possible eye problems from particles and droplets, and clinical problems due to particle and droplet inhalation into the respiratory passages follows. Chemical skin burns are discussed in Chapter 13.

### Eye Problems

The potential hazard to an astronaut's eyes of an atmospheric particle or droplet contaminant will be determined mainly by the physical and chemical characteristics, and the velocities of the particles or droplets. Non-chemical particles, referred to here as "foreign bodies", can irritate and injure eye tissues through a physical, or mechanical effect. Chemical particles cannot only act as foreign bodies but also, through a chemical effect, irritate and burn eye tissues. Chemical droplets can irritate and possibly burn.

As particles and droplets are accelerated by circulating air, they will become more hazardous to the eyes, for their impact frequency will increase and the "blink" reflex, which prevents approaching particles and droplets from impinging on the eyes, will become less effective. It is also thought possible that some particles and droplets might acquire a static

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\* In subsequent discussions, the terms "non-chemical particle" and "foreign body" are used interchangeably.

electrical charge and so might be attracted to the eye if in close proximity to it.

A brief discussion of the clinical features and the principles of treatment in space of possible eye problems caused by foreign bodies and chemicals follows. For more detailed coverage of this area, reference is made to the writings of Duke-Elder (12), Adler (1), Roper-Hall (46), Grant (19), Kuhn (34), Ryan (48, 49, 50), Zimmerman (60, 61, 62), and others (2, 53). A diagram of the sagittal section of the human eye is provided (Figure 8.1) to point out anatomical features of the eye which will be mentioned in the following discussion.

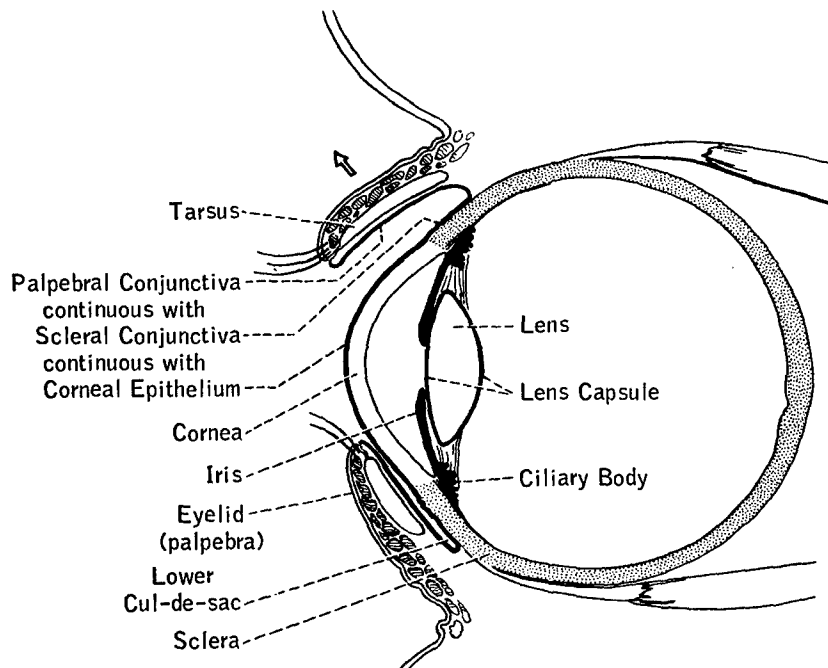


Figure 8.1 Sagittal Section of Human Eye.

### Foreign Bodies

Hairs, fibres, desquamated epithelium and small food and metallic particles should comprise most of the potential foreign body hazard to the eyes in space. Although the risk of meteoroid penetration of a spacecraft cabin is extremely low (Chapter 12), it should be pointed out that fragments of meteoroid and spacecraft wall from penetration will present a particularly

great hazard to the eyes because of their great number, high velocities, high temperatures, and rough or sharp shapes.

All eye problems caused by foreign bodies are usually accompanied by pain, lacrimation, and blepharospasm. It should be pointed out that in an emergency situation, temporary relief of these symptoms can be obtained by instilling a non-allergenic topical anesthetic such as 0.5 percent "Ophthaine" in the affected eye. However, one must assume the risks associated with leaving a foreign body either trapped under an eyelid or embedded in the cornea.

The trapping of foreign bodies under the eyelids will probably be the cause of most of the eye problems which occur in space. Most foreign bodies should only produce irritation. However, some with sharp edges or corners could actually injure the cornea or conjunctiva.

Fortunately, the majority of foreign bodies which get under the eyelids, especially the lower one, are either coated with mucus and automatically worked out by tearing and lid and eye movement, or removed by the well known method of overlapping the eyelids. On the other hand, it is possible that a trained astronaut might have to evert an eyelid to search for and remove a foreign body. Before undertaking this measure, pain and blepharospasm should be relieved by instilling a topical anesthetic. A foreign body under an eyelid can be removed with a cotton-tipped applicator moistened with saline, with cilia forceps or by one of the irrigation methods to be discussed under chemical eye problems. Although foreign bodies under the eyelids are usually removed by one of the above means, an occasional particle, especially if metallic or glass, can become embedded in either the palpebral or scleral conjunctiva. In this case, it is necessary to use a needle or eye spud for removal. Finally, special note should be made always to examine the lacrimal punctae when searching for foreign bodies in the eye in space, for it is considered possible that the risk of a short hair or fibre entering the eye and then being washed into and becoming firmly fixed in a punctum might be much higher in space than on Earth.

Such foreign bodies are easily removed with suitable forceps.

Any foreign body which becomes embedded in an astronaut's cornea will probably be a small single metal particle. Multiple foreign bodies could become embedded at the time of a meteoroid penetration, however.

The cornea should always be examined if no foreign body is found on searching under the eyelids, or if many foreign bodies could have entered the eye. Detection of a small embedded foreign body can usually only be accomplished with good illumination and magnification. Since the cornea is extremely sensitive, it is always necessary to instill a topical anesthetic before attempting to remove a foreign body embedded in it. A needle or eye spud should be used for removal, and the subsequent management of this injury accomplished in the manner outlined below for non-penetrating corneal injuries.

A ring of rust or debris may occasionally remain in the cornea after removal of a foreign body. This is most likely to occur if easily oxidizable metals, such as iron or copper are left embedded for a period of time. Unless superficial and easily removable in space, rust and debris should be allowed to remain in the cornea.

A foreign body embedded in the sclera is managed in the same way as one in the cornea. However, a scleral foreign body is usually more difficult to remove because of overlying conjunctiva and hemorrhage, neither of which are a problem in corneal foreign bodies.

The majority of non-penetrating injuries inflicted on the eyes by foreign bodies involve the cornea. Non-penetrating injuries of the sclera are managed similarly to those of the cornea. Conjunctival injuries are best left untreated.

An abrasion or wound of the corneal epithelium can result from a foreign body striking but not embedding in the cornea, or by a foreign body which is under the lid and is rubbing on the cornea. The wound remaining after an embedded corneal foreign body is removed is essentially similar to an abrasion. Fortunately this injury usually heals within 24 hours unless it becomes infected.

A rough or sharp foreign body which strikes the cornea at a high velocity or is trapped under a lid and rubs against the cornea could produce a laceration which is deeper than the corneal epithelium. Healing of this wound leads to scar formation and possibly a permanent visual defect, depending on the position, size, and density of the scar.

The diagnosis and determination of the extent of a non-penetrating corneal injury should be made first by staining the cornea with fluorescein. Use of a sterile paper impregnated with fluorescein (e. g., "Fluor-I-Strip" applicators) would be more practical in the weightless space environment than fluorescein solution. Then a bacteriostatic ointment, such as 10 percent sulfacetamide ointment, should be placed in the eye and a light, dry patch applied over closed lids. In 24 hours, the cornea should be stained and re-examined, and if healing is not complete but is progressing satisfactorily, the same treatment should be repeated. Also on this occasion, 5 percent homatropine might be instilled in the eye as a preventive measure for posterior synechiae and for the relief of pain due to inflammation of the iris.

If a non-penetrating injury of the cornea should become infected, a bactericidal ointment, such as chloramphenicol or "Neosporin" ointment, should be placed in the eye every three hours. As well, 1 percent atropine should be instilled one to three times daily. If possible in space, the frequent application of heat to the affected eye is also indicated.

A foreign body could strike the cornea or sclera of an astronaut's eye with sufficient velocity, as might be attained from a meteoroid penetration or explosion, to pierce these structures and enter the globe. The severity of penetrating injuries of the eye depends upon such factors as the size, temperature and inertness of the foreign body, and the tissues which are damaged during penetration. Some foreign bodies, such as plastics, sand, and glass, are quite inert. Corrosion-resistant nickel-base beryllium and aluminum alloys, and steel alloys containing chromium, vanadium, cobalt, nickel, titanium and boron incite little or no reaction with ocular tissues, usually becoming encapsulated over a period of time. On the other hand, corrosive alloys and various pure metals, such as copper, iron, zinc, and aluminum, react to a certain degree with ocular tissues, producing an

inflammatory reaction and ultimately visual impairment and perhaps even destruction of the involved eye.

Part of the iris prolapsed through a penetrating eye wound would not only be difficult to replace but also invite infection into the eye. Whenever the lens capsule is damaged, a traumatic cataract forms, leading to an impairment of vision. Such a cataractous lens can swell and, by blocking the angle of the anterior chamber of the eye, can cause secondary glaucoma.

An inflammatory process involving the uveal tract (iritidocyclitis) commonly occurs following a penetrating injury of the eye. It is characterized by deep-seated pain, photophobia, miosis and blurred vision. If the injury involves the region of the ciliary body, sympathetic ophthalmia, or a similar inflammatory process in the other eye may rarely occur, usually 2 weeks to 2 months after the injury. This extremely serious eye condition can progress on to complete loss of vision unless the injured eye is enucleated as soon as symptoms appear in the normal eye. No other treatment is definitely effective. Some cases have been controlled with rigorous local and systemic corticosteroid therapy (1, 59).

Because the skill and special instruments of the ophthalmic surgeon are required for the removal of an intraocular foreign body and for other emergency surgical procedures on the eye, it is doubtful if such procedures, except perhaps for enucleation will ever be carried out in space (52). Thus the risk of permanent blindness occurring from penetrating injuries will be somewhat higher in space than on Earth. It is thought that maximum possible supportive therapy may be adequate in most instances, however.

If a penetrating injury of an astronaut's eye is suspected, his visual acuity should be determined. Then his lids, sclera and cornea should be inspected for a small cut where a foreign body might have penetrated. This wound might be detected only by staining with fluorescein. It should be remembered that an eye suspected of having a penetrating injury should never be palpated and, of course, the astronaut should be warned to avoid rubbing his injured eye. Blood might be present in the anterior chamber of the eye, and the iris might be torn and the pupil irregular. Flattening

of the anterior chamber is an important sign of perforation. If x-ray facilities are ever placed on board spacecraft, every suspected case of foreign body penetration should be x-rayed.

Foreign bodies trapped under the eyelids, or embedded in the cornea or sclera should be removed. If part of the iris is prolapsed and cannot be replaced in the eye, it should best be excised with sterile scissors. Since it is thought that most penetrating foreign bodies in space will be reasonably sterile when they enter the eye, a local bacteriostatic agent might not be necessary <sup>(55)</sup>. One must keep in mind that such an agent in ointment form could itself be a dangerous foreign body if it enters the interior of the eye through the wound. However, if single or multiple foreign bodies have been removed, or other non-penetrating injuries are present, it might be wise to instill an aqueous bacteriostatic agent frequently in the eye. Prophylactic systemic antibiotic therapy is usually not indicated in such cases.

One percent atropine should be instilled every 8 to 12 hours in an eye penetrated by a foreign body, until healing appears complete and all signs and symptoms of inflammation have subsided. Both eyes should be patched except in critical operational situations when the best vision possible is required for a period of time. Except for eye examination, a local anesthetic should not be repeatedly instilled in an injured eye for the relief of pain. An analgesic or sedative will have to suffice.

An intraocular infection can result from the entry of bacteria through a penetrating wound, either at the time of or after penetration. As well as the treatment outlined above, local heat should be applied. Penicillin or a sulfonamide may be administered orally or by injection, but these drugs are frequently ineffective since they pass across the blood-aqueous barrier poorly <sup>(1, 55)</sup>. On the other hand, some success has been reported with chloramphenicol <sup>(54)</sup>.

The drug of choice in the treatment of secondary glaucoma has been a carbonic anhydrase inhibitor, such as acetazolamide. Of interest is the success reported with intravenous dehydrating agents <sup>(10, 18, 23, 58, 59)</sup>. The possible potential usefulness of them in space has been discussed in Chapters 1, 2, 4, and 14. These agents are apparently effective in the



treatment of acute glaucoma of both the primary and secondary types, and may also aid in the absorption of blood out of the anterior chamber. Mannitol has been the preferred dehydrating agent. A carbonic anhydrase inhibitor drug can be used in conjunction with a dehydrating agent. In some instances, especially where the glaucoma is primarily due to hemorrhage, the frequent instillation of a miotic drug, such as 1/2 to 4 percent pilocarpine, to maintain continuous pupillary constriction may be indicated. On the other hand, it may be advisable to instill instead a cycloplegic drug, such as 1 percent atropine, if severe inflammation supervenes. The selection of such drugs requires sound clinical judgment based on extensive ophthalmologic experience. Hence consultation with an Earth-based ophthalmologist will be a must if such a situation should develop in space.

### Chemicals

The severity of any chemical injury of the eyes will depend on various factors, such as the type, concentration and physical nature of the chemical, and the duration that the eyes are exposed to the chemical. It should be remembered that solid reactive chemical particles can produce mechanical injuries of the eyes as well as severe local burns.

Alkaline chemicals are a much greater threat to the eyes than any other chemical <sup>(48)</sup>. The greatest degree of damage apparently occurs between pH 11 and 12 <sup>(48)</sup>. Alkalis penetrate the eye tissues rapidly, producing deep burns and all of the possible complications of severe eye burns discussed below. On the other hand, serious injuries from acids rarely occur above pH 2.5 and are often limited to the epithelium <sup>(48)</sup>. Accordingly, serious complications are less likely to occur following mild exposures to acids than to alkalis. Eye injuries caused by other classes of chemicals have been discussed by Ryan <sup>(48, 49, 50)</sup> and Grant <sup>(19)</sup>.

Every effort must be directed at minimizing the use of hazardous chemicals in space and at maximizing the safety factors if such chemicals are required. The probability of carbon dioxide absorbents, such as lithium hydroxide and sodium superoxide, becoming a threat to the eyes might be greatly increased if environmental control systems require servicing in

space. These absorbents are alkalis which, as mentioned above, are extremely damaging to the eyes. As well, they tend to change from pellet to powder form as they are utilized. It is noted again that most analytical systems will employ hazardous chemicals which could be spilled at the time of replacing spent chemicals or servicing a system, or during analytical procedures.

Various degrees of injury, from a temporary mild inflammation to a severe burn of the extraocular tissues could be possible if a hazardous chemical should come into contact with an astronaut's eyes in space. A mild injury is accompanied by lacrimation, an itching or burning sensation, and blepharospasm. A severe burn is accompanied by lacrimation, burning pain, blepharospasm, and congestion, edema and possibly immediate necrosis of extraocular tissues.

Perforation of the globe is possible with deep burns. Injured eye tissues are very susceptible to infection, which would enhance the degree of damage and delay healing. Other serious early complications which may follow a seemingly mild chemical burn are iridocyclitis and secondary glaucoma.

A burn involving the subepithelial tissue of the cornea will heal by scar tissue formation and ingrowth of vascular tissue, leading to some degree of impaired vision. A severe burn of the palpebral conjunctiva can be followed by marked contraction of this tissue, resulting in inversion of the lid (entropion). A severe conjunctival burn can also lead to the formation of adhesions between the eyelids and the globe (symblepharon). Scarring of the outer surface of the lids can result in lid eversion (ectropion).

If a harmful chemical should come into contact with the eyes of an astronaut in space, his eyes should be irrigated as soon as possible with copious amounts of water or, if as readily available, isotonic saline or other more physiologic solution. Special buffering agents available for the irrigation of eye injuries, which could be produced by specific chemicals carried on board the spacecraft, might be applicable in the space situation. Irrigation is usually continued for at least 20 to 30 minutes for alkalis or other

severely damaging chemicals. For more innocuous chemicals, as little as 10 minutes irrigation may suffice.

Irrigation of an eye will be difficult in the weightless environment. However, no adequate procedure can be substituted for irrigation. It is suggested that with water-absorbing material around the eye, a suction vent near the eye, and the water or saline directed in a suitable stream at the eye, irrigation of the eye should be accomplished in space without creating a droplet hazard. An eye cup with water circulating through it might be another method of irrigation to be considered. In order to relieve pain and blepharospasm, and so facilitate irrigation under the lids, a local anesthetic can be rapidly instilled in the eye just prior to or after having started irrigation. The lids should be held open during the irrigation, so that the solution reaches all parts of the conjunctiva and cornea. In order to be assured that all chemical, particularly if in solid form, has been removed from the eye, each eyelid should be completely everted and the posterior surface of the cul-de-sac irrigated. Solid particles can also be removed from the eye with a moist cotton-tipped applicator or suitable forceps.

After irrigation, the cornea and conjunctiva should be stained with fluorescein and carefully examined, under magnification if possible, in order to determine the severity of injury and, if applicable, detect any small chemical particles which still remain in the eye. The importance of examining the under-surfaces of the lids and cul-de-sacs cannot be overemphasized.

All chemical burns of the surface of the eye should be treated with an ointment or water-soluble preparation which includes both a bactericidal agent and a cortisone derivative (e.g., "Neodeltacortef", "Neodecadron"). Authorities agree that the beneficial effect of a cortisone derivative, especially in minimizing the inflammatory reaction, and corneal scarring and vascularization, far outweighs the potential risk of this agent causing aggravation of a possible ocular viral disease. The ointment preparation and a mydriatic drug, such as 5 percent homatropine or 1 percent atropine, should be placed in the eye every 8 to 12 hours if a patch is to be applied. If the injury is mild or if the eye must be left open, a water-

soluble preparation would be preferred, instilled in the eye at least every one to 2 hours. A topical mydriatic drug is a necessity for all corneal injuries of any significant degree, for it will do much to prevent extension of corneal inflammation to the iris and ciliary body, and to prevent severe ache from iris and ciliary muscle spasm.

A dry patch should be applied to most mild and all severe chemical burns. The patch immobilizes the lids in a closed position, which tends to exclude contamination and minimize mechanical trauma. The repeated use of local anesthetics in the eye is contraindicated, for such agents can delay healing and may even increase damage. If possible in space, the local application of cold may help to prevent or reduce congestion, edema, and pain. An analgesic drug should be given as required.

One of the most common complications of chemical burns of the eye is the adherence of the palpebral to the scleral conjunctiva if they are badly damaged. The topical ointments mentioned above may prevent this adherence to some degree. However, it may be necessary to break down adherent points under local anesthesia daily with a suitable instrument such as a smooth glass rod.

The secondary glaucoma which sometimes develops after chemical burns, especially from alkaline agents, is usually very difficult to control. Foremost in the treatment of this kind of glaucoma is the administration of an oral carbonic anhydrase inhibiting drug, such as acetazolamide. A topical cycloplegic, such as 1 percent atropine, also can be used, but it seldom is effective enough to control severe glaucoma by itself. Use of miotics seems unattractive because of the possibility of increasing discomfort and allowing posterior synechiae to form <sup>(19)</sup>.

Definitive treatment of complications such as corneal scarring and vascularization, conjunctival scarring and symblepharon, entropion and ectropion of the lids, and secondary glaucoma which has not responded to drug therapy, demand the skill and instruments of the ophthalmic surgeon. Hence it is doubtful if such treatment will ever be possible in space.

## Respiratory Tract Problems

### Predictions

Busby and Mercer have predicted what the characteristics of particle and droplet inhalation into and deposition in the respiratory tract will be in the weightless environment <sup>(8)</sup>. The medical implications to be drawn from this study, which is summarized below, serve as a basis for discussing various respiratory problems which are considered most likely to occur in space.

The first question which arose was whether or not suspended particles or droplets of sizes up to that which can enter the nasal passages or mouth can be inhaled if they come into contact with the inspiratory air stream. Air flow and particle or droplet size were related in the equation:

$$u=v\left(1-e^{-\frac{3.42 \times 10^5 t}{d_a^2}}\right)$$

which gives the velocity,  $u$ , which a particle or droplet of aerodynamic diameter\*,  $d_a$  microns, might have,  $t$  seconds after it is introduced into air flowing at velocity,  $v$ . This relationship is illustrated graphically in Figure 8.2, which shows the times required for particles or droplets of various aerodynamic diameters to reach one-half of an air velocity.

From this relationship it was predicted that particles and droplets of sizes having an aerodynamic diameter less than a few hundred microns, if in the inspiratory air stream, will approach the velocity of the inspiratory air stream so rapidly that for all practical purposes, the concentration and distribution of such particles and droplets which enter the nose or mouth during a normal

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\* "Aerodynamic diameter" of a given particle or droplet means the diameter of a sphere of unit density having the same settling velocity as the particle or droplet at room temperature and pressure.

inspiration will not be significantly different from that in the spacecraft cabin atmosphere.

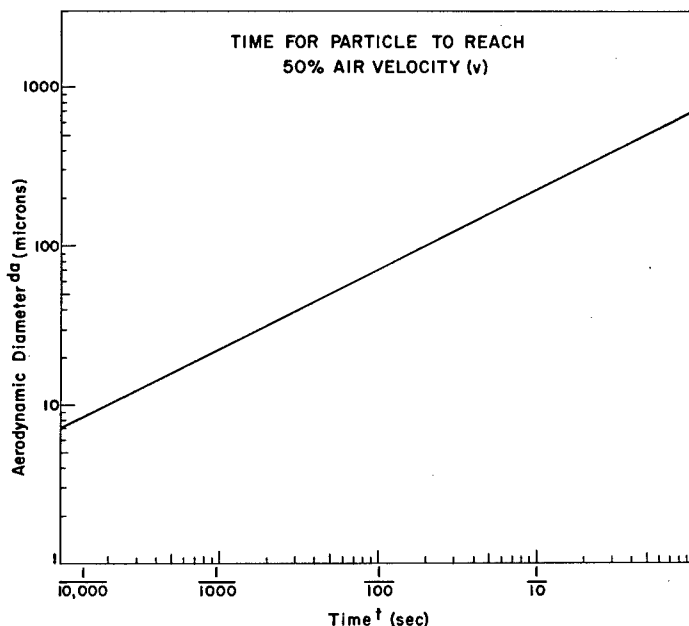


Figure 8.2 Time for Particles or Droplets of Various Aerodynamic Diameters to Reach 50% of Air Velocity ( $v$ ).

(After Busby and Mercer <sup>(8)</sup>)

Since gravity is a factor in determining the particle and droplet deposition in the respiratory passages, the other question which had to be answered was what the characteristics of particle and droplet deposition in the respiratory passages might be in the weightless environment. Mercer <sup>(40)</sup> had modified and extended the method first employed by Findeisen <sup>(15)</sup> to calculate values for the deposition of various aerodynamic diameter particles or droplets in the respiratory passages in the Earth (unit gravity) environment, and had shown that these values compared quite favorably with available experimental data. To consider the analogous situation that would exist in the space (weightless) environment, it was only necessary to discount in such calculations that contribution made to deposition by sedimentation, which is due to gravity.

The characteristics of aerodynamic diameter particle or droplet deposition in the respiratory passages in the Earth (unit gravity) and space (weightless) environments are demonstrated by the "deposition curves" in Figures 8.3 to 8.5. All curves were calculated for nasal breathing, a tidal volume of 750 cc and a respiratory rate of 15 breaths per minute. It is noted that even though these curves are for nasal breathing, available experimental evidence suggests that the efficiency of the mouth as a filter is similar to that of the nose, providing an individual breathes through his mouth in a normal manner <sup>(41)</sup>. Air at 14.7 psia is breathed in the Earth situation. Since the current literature supports the use of reduced atmospheric pressures and thus increased oxygen concentrations in spacecraft cabins, calculations were made on the basis of an inhaled gas mixture composed of 50 percent nitrogen-oxygen at a total pressure of 7.0 psia (362 mm Hg). Even though the viscosity of the respired gas is altered by the relative amounts of nitrogen and oxygen, the effect of this change on the "deposition curves" appears to be negligible <sup>(41)</sup>.

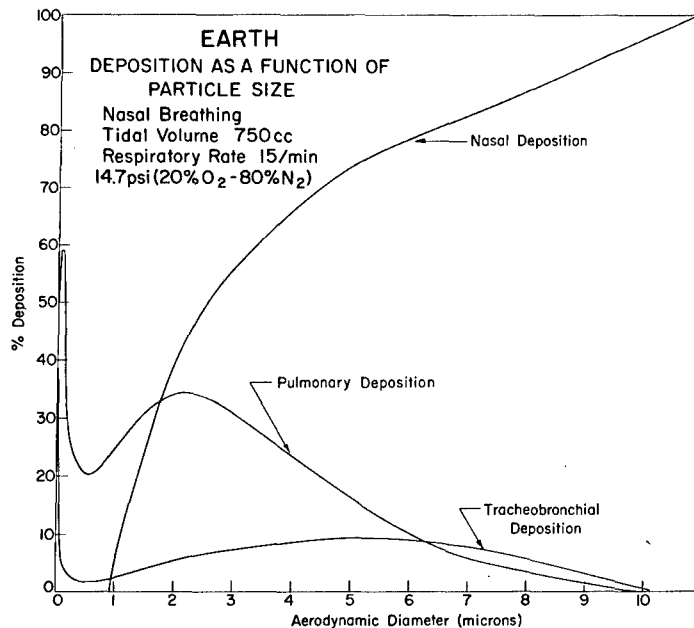


Figure 8.3 Deposition as a Function of Particle or Droplet Size in the Earth (Unit Gravity) Environment.

(After Busby and Mercer <sup>(8)</sup>).

As well, it is believed that the substitution of helium or another inert gas for nitrogen would alter viscosity by only a few per cent, and hence should not alter these "deposition curves" significantly.

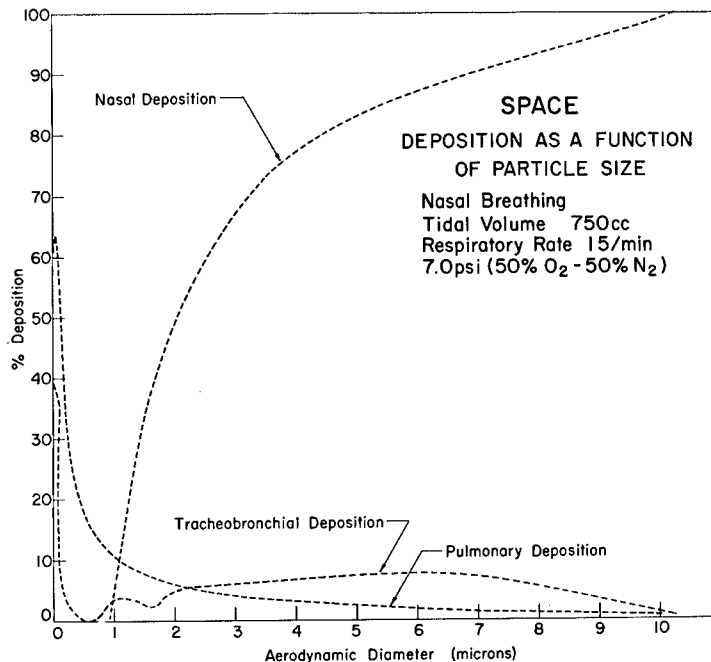


Figure 8.4 Deposition as a Function of Particle or Droplet Size in the Space (Weightless) Environment.

(After Busby and Mercer <sup>(8)</sup>).

For considerations of the pattern of deposition, the respiratory tract was divided into nasal (or nasopharyngeal), tracheobronchial and pulmonary regions. The subregions of the airways and their dimensions are shown in Table 8.2. The tracheobronchial region includes all the ciliated airways (including the larynx), which are assumed to terminate at the distal ends of the terminal bronchioles. The pulmonary region includes the distal respiratory passages such as the respiratory bronchioles, and alveolar ducts and sacs. It is also pointed out that in the discussion which follows, the term "upper respiratory passages" refers to the nasal (or oral) regions of the respiratory passages, and the term "lower respiratory passages" refers to the tracheobronchial and pulmonary regions.



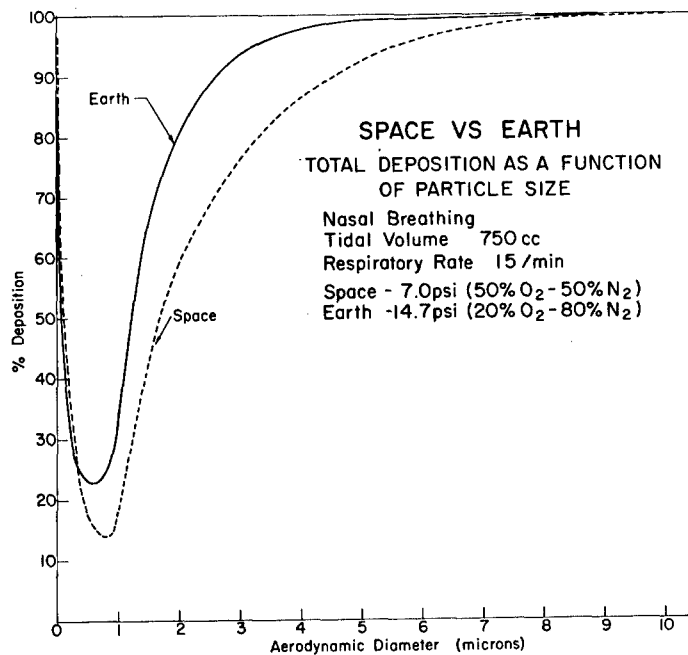


Figure 8.5 Total Deposition as a Function of Particle or Droplet Size in the Earth (Unit Gravity) and Space (Weightless) Environment.

(After Busby and Mercer <sup>(8)</sup>).

A number of medical implications can be drawn from these predictions of the characteristics of particle and droplet inhalation into and deposition in the respiratory passages in the weightless environment. It is assumed here that all particles and droplets will tend to follow the same predicted pattern of inhalation into and deposition in the respiratory passages that would be expected to standard "aerodynamic diameter" particles.

The tendency for particles and droplets to remain suspended in the weightless environment and the predicted characteristics of particle and droplet inhalation into the respiratory passages in the weightless environment imply that the amount of particle or droplet contaminant which an exposed astronaut might inhale could be markedly increased, possibly by several orders of magnitude, over the amount that can be inhaled if the same contaminant is introduced in a similar situation into a unit gravity environment. The

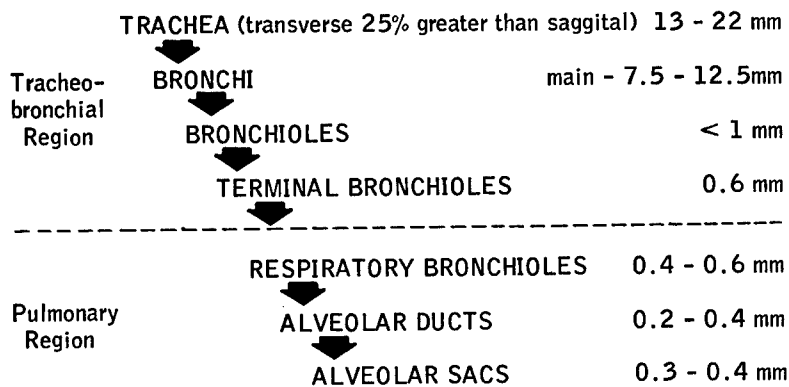


Table 8.2 Internal Diameters of the Respiratory Passages in the Tracheo-bronchial and Pulmonary Regions of the Adult Lung.

(After Findeisen <sup>(15)</sup>, Landahl <sup>(36)</sup>, Sander <sup>(51)</sup>, von Hayek <sup>(56)</sup>, and Weibel <sup>(57)</sup>).

predicted characteristics of particle and droplet deposition in the respiratory passages in the weightless environment show that in space, as on Earth, the nose or mouth should continue to operate as highly efficient filters, protecting the lower respiratory passages from all particles and droplets above about 10 microns in diameter. Fortunately, this size is considerably less than that of particles and droplets of most of the aforementioned contaminants which might be introduced into the spacecraft cabin atmosphere. In this respect, it should be pointed out that the use of powdered chemicals of particle sizes greater than 10 microns in space would be an important safety measure.

It must still be considered possible, however, for an astronaut to be exposed to particles (e.g., aggregates of smoke and fume particles) and droplets (e.g., liquid ejected as a fine spray) less than about 10 microns in diameter. The "deposition curves" predict that fewer inhaled particles and droplets between about 0.5 and about 10 microns in diameter will be deposited in the lower respiratory passages, especially in the pulmonary region, in the weightless as compared to the unit gravity environment. This implies that weightlessness might offer some protection to an astronaut from

certain contaminants which, if inhaled in a similar concentration in a unit gravity environment, would be irritating to or damage alveoli and respiratory bronchioles, or produce systemic toxic effects by being absorbed. It is of interest to note that weightlessness exerts its greatest protective effect in the pulmonary or non-ciliated region of the respiratory passages -- a region where deposited contaminants are not moved out of the respiratory passages by ciliary action. This predicted decrease of particle and droplet deposition in the pulmonary region in the weightless as compared to the unit gravity environment implies that the concentration of particles and droplets one micron in diameter inhaled into the respiratory passages in the weightless environment could be approximately doubled before the percent deposition of such contaminants in the pulmonary region in this environment would be equivalent to their percent deposition in the unit gravity environment. Similarly, the inhaled concentration of particles, and droplets could be increased by approximately 6 times for particles and droplets 2 microns in diameter, 7 times for those 3, 4, and 5 microns in diameter, 6 times for those 6 microns in diameter, 5 times for those 7 and 8 microns in diameter, and 3 times for those 9 microns in diameter. However, even though it is predicted that the pulmonary deposition of inhaled particles and droplets between about 0.5 and about 10 microns in diameter will be significantly reduced in the weightless environment, one must remember that such contaminating particles or droplets could still be suspended in a concentration which would be harmful.

Since the weightless environment does not alter the high percent deposition of particles and droplets below about 0.5 microns in diameter in the lower respiratory passages, the consequences of inhaling such contaminants will not be different in the weightless as compared to the unit gravity environment. Contaminants of this size are most likely to be in the form of fumes or smoke. Since particles or droplets below 0.9 microns in diameter will apparently not be deposited in the nasal (or oral) regions of the respiratory passages, their inhalation should not produce clinical problems in the upper respiratory passages. On the other hand, because of the very high percent deposition of particles and droplets below about 0.5 microns in diameter, tracheobronchial and pulmonary tissues could be severely irritated

or damaged.

From the equation which illustrated the relationship between air flow and particle size, Busby and Mercer concluded that the concentration and distribution of particles and droplets of diameters up to a few hundred microns which will enter the nose or mouth in the inspiratory air stream will not be significantly different from that in the spacecraft cabin atmosphere <sup>(8)</sup>.

Whether or not particles or droplets larger than a few hundred microns in diameter (e.g., several hundred microns to 1 cm) can be inhaled will depend less on particle and droplet size, and more and more on such important factors as particle or droplet shape and density, their spatial relationship to the inspiratory air stream and mouth and nasal openings, their velocities and directions of movement relative to an astronaut, the velocity-time profiles of the inspiratory and expiratory air streams, and the duration of the pause between inspiration and expiration. Taking all of these factors into consideration, it is predicted that various particles, especially those of low density particles, and droplets of possibly up to 1 cm in diameter, could be inhaled in the weightless environment. Accordingly, it is thought that as compared to on Earth, an astronaut in space might run a somewhat higher risk not only of inhaling large particles and droplets into his nose and mouth, but also of aspirating large particles and droplets into his lower respiratory tract. For aspiration to occur, it must be assumed that normal mechanisms, such as coughing, swallowing and reflex glottic closure, which exclude large particles impacting in the oropharynx from the larynx might not always be effective, especially if an astronaut should inhale several large particles or droplets at one time or if his exposure to and inhalation of the contaminant occurs unexpectedly. An inspiratory gasp, which produces high air velocities, might occur from an astronaut being "startled" or "stimulated" by an inhaled contaminant and could, therefore, increase the risk of the contaminant being aspirated. Because a much larger particle or droplet can enter and pass through the mouth than the nasal passages, aspiration is much more likely to occur if an astronaut is

breathing through his mouth.

### Acute Chemical Inflammation of the Upper Respiratory Tract

The inhalation into the nose of a particulate chemical, such as lithium hydroxide or a superoxide used in environmental systems, or a liquid chemical, such as an acid or alkaline reagent used in an analytical system, could lead to a severe non-specific inflammation of the sensitive lining of the nose and pharynx, or so-called acute chemical rhino-pharyngitis. Considered much less likely to occur following inhalation of a chemical, severe chemical inflammation of the lining of the mouth is managed in a similar fashion to that of the nose.

The initial response to a chemical deposited in the nose is vasoconstriction. This is accompanied by symptoms ranging from an itching-burning sensation to severe pain. Within minutes, however, vasodilatation occurs. The hyperemic nasal mucosa rapidly becomes edematous and secretes a watery fluid. This response can manifest clinically as a feeling of fullness or tightness in the nose and sinus regions, nasal obstruction, a profuse watery discharge, a "sore throat", lacrimation and continued sneezing. The lining of the nose and pharynx can undergo some degree of localized or diffuse, immediate or delayed necrosis, particularly if larger chemical droplets or particles are inhaled. In this case, the nasal discharge is in the form of an exudate, which is opaque and viscous. It can be blood-streaked and contain pieces of necrotic intranasal tissue. Frank nasal and pharyngeal bleeding may occur up to several days after the incident.

The most common sequela of acute chemical rhino-pharyngitis is secondary infection of the damaged nasal and pharyngeal lining. The nasal discharge becomes purulent and remains so until the continuity of the ciliated epithelium is restored. Severe infections are usually accompanied by fever and general malaise. The remote possibility of secondary bacterial invaders producing disorders of serious consequence, such as sinusitis, otitis media, mastoiditis, meningitis, osteomyelitis, and brain abscess, should be kept in mind.

The treatment of acute chemical rhino-pharyngitis has been suggested by Fischer <sup>(16)</sup> and Kilgore <sup>(33)</sup>. As soon as possible after inhaling a

chemical into his nose, an afflicted astronaut should use any method possible to irrigate his nose and pharynx. Water or, if available, isotonic saline or any other isotonic solution should be flushed in and out of his nose and gargled. Irrigation should be continued for several minutes or until the initial irritation has subsided. It might be carried out for many minutes if he inhales large particles which could be impacted in his nose.

It is debatable as to whether or not to instill immediately a potent, rapid-acting, topical vasoconstrictor, such as 1/1000 epinephrine, in a chemically-inflamed nose. On the one hand, such an agent would, by shrinking the nasal lining, allow better nasal irrigation and possibly less absorption of a toxic chemical into the body. On the other hand, one must keep in mind the damage which would be incurred by a chemical while waiting for a vasoconstrictor to take effect. Accordingly, it is thought that vasoconstriction should be attempted after some irrigation has been carried out.

As will be pointed out in the discussion of acute chemical inflammation of the lower respiratory tract, steroid drugs appear to have an excellent anti-inflammatory action on the respiratory tract mucosa. Therefore, it is suggested that suitable steroid preparations be administered as indicated both intravenously (e.g., hydrocortisone sodium succinate) as soon as possible after an astronaut inhales a chemical agent, and instilled in his nose (e.g., 1 percent hydrocortisone acetate) after irrigation. An oral steroid (e.g., methylprednisolone) might be given for several days to serious cases.

Control of nasal bleeding secondary to chemical damage can usually be accomplished without any special treatment or with the very simplest of measures. Since bleeding is most likely to occur from the anterior part of the nasal septum, a cotton pledget should be placed in the front of the nasal cavity and pressure applied to the nose to compress it against the septum. Soaking the pledget with a vasoconstrictor, such as 1/1000 epinephrine, or the local application of a hemostatic agent, such as "oxycel", "gelfoam" or topical thrombin might be required to arrest bleeding. Finally, nasal packing is a specialized procedure which is rarely required for persistent nasal bleeding <sup>(6)</sup>.

If the lining of the nose has been extensively denuded by a chemical, the raw surfaces should be covered with petrolatum gauze to prevent the formation of adhesions. This dressing should be changed every 2 to 3 days until the areas are re-epithelialized. A suitable broad spectrum antibiotic should be administered by the oral or intramuscular route if infection of damaged nasal or pharyngeal tissues occurs. Finally, it should be noted that an analgesic or sedative drug might be required by a serious case of acute chemical rhino-pharyngitis.

### Intranasal Foreign Body

An astronaut could inhale a non-chemical particle which, because of its size and shape, might become impacted in the nasal cavity rather than being expelled by sneezing or escaping in secretions. Food, metal and plastic particles are examples of such possible foreign bodies.

A small smooth foreign body in the nasal cavity could give little or no discomfort <sup>(29)</sup>. As a result, its presence might remain undetected until ulceration of the nasal mucosa occurs from mechanical and possibly some chemical irritation. The clinical manifestations of mucosal involvement may appear from days to weeks after the foreign body enters the nose. They are characterized at first by a unilateral serous discharge, then an odorous, purulent discharge. Blood streaking of the discharge or frank bleeding could occur.

No foreign body should be allowed to remain in an astronaut's nasal cavity, for it could produce necrosis and secondary infection of nasal tissue or be aspirated into his lower respiratory tract <sup>(6)</sup>. With good illumination and a nasal speculum, either the foreign body itself or an accumulation of secretion at its site of location will be seen. Better visualization and possibly facilitated removal of the foreign body might be accomplished by shrinking the nasal mucosa with a topical vasoconstrictor, such as 1/1000 epinephrine <sup>(29)</sup>. The majority of foreign bodies in the nasal cavity should be located in the anterior part of the nasal cavity or in the inferior meatus along the floor of the nose. If ever possible in space, an x-ray of the nasal passages for the location of a foreign body might on occasion prove useful.

An intranasal foreign body can be removed using an open-ended suction tip or cotton-tipped applicator, a blunt bent probe and a suitable forcep, such as an alligator forcep. Care must be taken to avoid pushing, or having an astronaut inadvertently suck a foreign body into his pharynx, from which the foreign body might be aspirated. Measures which might be taken to control secondary bleeding are discussed above. A suitable broad spectrum antibiotic should be administered as indicated for infection.

### Aspirated Foreign Body

The aspiration of a non-chemical particle into the lower respiratory tract in space can lead to a number of serious clinical problems which have been discussed so well in the vast literature on this area. Particular reference is made to the excellent reviews of Jackson and Jackson (28, 29, 30), Hollinger (24, 25, 26, 27) and other authors (3, 7, 9, 13, 14, 17, 38, 39, 42, 43, 45) for greater detail than that to be presented below.

Generally speaking, both the clinical manifestations produced by an aspirated foreign body and the times of appearance of these manifestations are highly variable, depending in most cases on the site where the foreign body lodges, the degrees of primary obstruction and irritation that it produces, and the length of time that it remains in the lower respiratory tract. These factors are determined in readily apparent ways by the size, shape, and chemical activity of the foreign body. It is also possible that an aspirated foreign body in space could be microbiologically contaminated, and thus serve as a nidus for infection.

In the light of the above considerations, it is understandable how a non-irritating, non-obstructing foreign body such as a smooth particle of an inert metal, glass, or plastic can remain lodged for months to years in the lower respiratory tract without giving rise to clinical manifestations (5, 21, 44). In the majority of instances, however, the consequences of obstruction of the laryngeal, tracheal, or bronchial passages by a foreign body ensue. Signs and symptoms may appear immediately if obstruction of a passage is complete. They may present after a quiescent period of days to weeks during which, through mechanical and chemical irritation, the foreign body causes



localized mucosal swelling that perfects the occlusion of the passage. Characteristically, the delayed periods are shortest in cases of aspirated vegetal foreign bodies, for all vegetal substances irritate the respiratory tract mucosa by chemical action, producing a violent laryngotracheo-bronchitis and obstructive swelling <sup>(14)</sup>. On the other hand, clinical manifestations from aspirated metallic foreign bodies often take many weeks to many months to appear, even if these foreign bodies are initially rough and obstructive or become so by corrosion, or produce some chemical irritation through corrosion.

A foreign body in the larynx of an astronaut will produce paroxysms of violent coughing, gagging, choking and wheezing. An obstructing foreign body may cause immediate death unless coughed out. Lodgment of a non-obstructing foreign body can produce any one or more of the following signs and symptoms: hoarseness, croupy cough, stridor, wheezing, dyspnea, pain, aphonia, hemoptysis, and a subjective feeling of the presence of the foreign body in the larynx. Often a small non-obstructing foreign body may become asymptomatic for a period of time. Any foreign body remaining in the larynx is potentially dangerous, however, for secondary inflammation can produce fatal edema of the larynx, and secondary infection can destroy laryngeal tissues and lead to grave consequences by spreading out into the tissues of the neck and down into the mediastinum.

The presence of a foreign body in an astronaut's larynx is in most cases apparent from his history alone. Confusing the diagnosis, however, might be laryngeal symptoms persisting from trauma caused by a foreign body that has passed on into deeper respiratory and food passages, or by one that has been coughed out. Therefore, indirect laryngoscopy and rarely, if possible on board the spacecraft, an x-ray are required for confirmation. Since direct laryngoscopy requires special skills and instruments, and often general anesthesia, this procedure is not considered possible in space in the foreseeable future. It should be remembered that a foreign body which is not found in the larynx could be resting temporarily in deeper respiratory passages without producing symptoms.

A non-obstructing foreign body in the larynx is usually coughed out

within minutes. The simplest maneuver, such as a slap on the back during an expulsive effort, may sometimes assist to dislodge a foreign body (38). If an astronaut's larynx is obstructed or suffocation is threatening, an immediate tracheostomy must be performed. It is pointed out that if this surgical procedure cannot be performed immediately, life-sustaining ventilation of the lungs can be achieved temporarily by inserting a large-bore needle (e.g., 16 gauge needle) through the cricothyroid membrane. If efforts at expelling a foreign body are unsuccessful, it should be withdrawn as soon as possible with suitable forceps and indirect laryngoscopy. This procedure is rendered comparatively easy if a suitable topical anesthetic, such as 10 percent cocaine or 2 percent xylocaine, is applied to the laryngeal mucous membrane, epiglottis and base of the tongue prior to attempting removal. It is possible that disimpaction and possibly removal of a foreign body might be carried out by way of a tracheal wound previously made for the relief of airway obstruction. Extreme care must be taken to prevent a foreign body in the larynx from being dislodged during removal and entering the deeper respiratory passages. Other possible measures in the treatment of a foreign body in the larynx in space are supportive. A broad spectrum antibiotic may be indicated if infection ensues. If the foreign body cannot be removed in space, a more permanent tracheostomy might be required until direct laryngoscopic removal can be performed on Earth. Measures might be needed for post-hypoxic cerebral edema resulting from the temporary asphyxia (Chapter 1).

Usually a foreign body in the trachea initially produced paroxysms of coughing as well as one or more of the following manifestations: a chronic cough, hoarseness, dyspnea, cyanosis, and a slapping feeling on inspiration and expiration. A large foreign body may completely obstruct the trachea and, in spite of possible immediate attempts to remove the foreign body through a tracheostomy wound, may cause death in a few minutes. A foreign body remaining in the trachea is potentially dangerous. Irritative inflammation, especially from vegetal foreign bodies, can result in fatal obstructive swelling or severe laryngotracheobronchitis. Secondary infection may produce a fatal mediastinitis or pneumonitis.

If elicited, a history of initial choking, gagging, and wheezing will be helpful in the diagnosis of a foreign body in the trachea. The pathognomonic signs of a foreign body in the trachea are an "audible slap" heard at the mouth and a "palpable thud" felt over the larynx, created as the foreign body is trapped at the larynx by the vocal cords during a cough or forced expiration (28, 29, 30). A wheeze is usually heard when the foreign body lodges somewhere in the trachea and becomes stationary. If ever possible on board the spacecraft, an x-ray might make or confirm the diagnosis.

A non-obstructing foreign body in the trachea is often coughed out within minutes. This might even be more the case in the absence of gravity which tends to pull a foreign body back down into the trachea. The removal of a tracheal foreign body should be attempted immediately through a tracheostomy wound if it is obstructing or threatening suffocation. Bronchoscopic removal is a highly skilled procedure which will probably not be performed in space in the foreseeable future. Removal of a tracheal foreign body might be attempted through a tracheostomy wound if expulsive efforts fail and if it is thought that disastrous sequelae could occur prior to returning to Earth. Otherwise, only supportive forms of therapy, such as a broad spectrum antibiotic for infection and an antitussive agent for chronic cough, might be given. Measures might also be required for post-hypoxic cerebral edema resulting from temporary asphyxia (Chapter 1).

The initial symptoms produced by a foreign body in a bronchus are coughing, asthmatoïd wheeze and others mentioned above. At once or after a symptomless interval, a productive cough, blood-streaked sputum, metallic taste, odor of the foreign body, fever, and malaise may be present due to decomposition of the foreign body and the pathologic sequelae it produces. As was pointed out above, non-obstructing relatively inert foreign bodies can be asymptomatic for weeks, months, or even years. On the other hand, obstruction of a bronchus is followed by atelectasis of the portion of the lung supplied by the bronchus, after which suppurative manifestations such as lung abscess, empyema, bronchiectasis, and pneumonia might ensue. Such sequelae can also result from prolonged partial obstruction

from swelling of the mucous membrane or growth of granulation tissue at the site of the foreign body <sup>(42)</sup>. It is pointed out again that vegetal foreign bodies are markedly irritating by chemical action. They produce a violent laryngotracheobronchitis with signs and symptoms of toxemia, cough, dyspnea, cyanosis, and irregular fever. Finally, a sharp foreign body or one that produces an obstructive emphysema can cause a disruption of pulmonary structure, with complications such as a sudden pneumothorax, mediastinal emphysema extending often into the neck, or acute mediastinitis being possible <sup>(17, 39)</sup>.

The diagnosis of a foreign body in a bronchus of an astronaut will in most cases be made from the initial symptoms and the physical findings to be outlined below. Occasionally, however, the diagnosis might only be based on a high index of suspicion and a careful history, for manifestations produced by the foreign body may not appear until long after an episode of choking or coughing, at which time the possibility of a foreign body passing into a bronchus was not considered. If ever possible in space, an x-ray would be valuable not only in making or confirming the initial diagnosis but also for diagnosing sequelae and the response of these sequelae to therapy. The physical signs will vary with the conditions present in different cases and at different times in the same case. Secretions, both normal and pathologic, may shift from one location to another. The foreign body may change position, admitting more, less, or no air into a lung or lung segment. It may shift to a new location in the same lung or even in the other lung. The signs of diagnostic importance are chiefly those of partial or complete bronchial obstruction. They are classically described as follows <sup>(29, 30, 42)</sup>:

If obstruction is partial, there is usually a persistent sonorous rhoncus, more conspicuous during expiration. In cases with equal air entry and air exit past the site of the obstruction, a rhoncus and occasionally a small patch of rales over the position of the foreign body may be the only signs. In cases with inadequate air entry but adequate air exit, partial collapse of the lung occurs, associated with dullness, diminished breath sounds and rales. In cases with adequate air entry but inadequate air exit, obstructive emphysema is produced, with hyper-resonance and diminished breath sounds being noted over the involved lung.

If a major bronchus has been entirely occluded, there are the usual signs of an obstructed lobe or lung, such as dullness to percussion, diminished fremitus, absence of breath sounds and usually some degree of mediastinal displacement.

Past experience has shown that only about 3 percent of foreign bodies in bronchi are coughed up spontaneously, the remainder having to be removed by bronchoscopy (28, 29). Since bronchoscopy is a highly skilled procedure which is unlikely to be performed in space in the foreseeable future, appropriate supportive therapy will have to suffice until an astronaut returns to Earth. With a suitable broad spectrum antibiotic, the septic sequelae should be adequately controlled. As will be discussed under acute chemical inflammation of the lower respiratory tract, steroid therapy might be of some value in treating cases with fulminating laryngotracheobronchitis due to vegetal foreign body.

Even in cases of profound sepsis, the prognosis for complete recovery following removal of a foreign body which has been in a bronchus for a prolonged period of time is fortunately excellent. Jackson and Jackson point out that 95 percent of cases of foreign body of other than vegetal origin completely recover (30). This figure and the unstated poor prognosis of cases of vegetal foreign body would no doubt be bettered by therapy given immediately as indicated.

#### Acute Chemical Inflammation of the Lower Respiratory Tract

An acute non-specific inflammation of the lower respiratory passages of an astronaut might occur if he inhales an irritant gas or chemically-irritating particles or droplets which are small enough to be inhaled beyond the nasal or oral regions of his respiratory passages. It might also result from the aspiration of chemically-irritating particles or droplets. Possible contaminants fitting into the first category are gases formed by the chemical breakdown of metals, plastics, and other materials by spilled acids and alkalis. Examples in the second category are: chemical dusts, especially if powdered chemicals are used on board spacecraft; fumes and smokes formed by the pyrolysis or combustion of plastics, metals and other materials; and chemical mists which might be formed if acids or alkalis are sprayed into the spacecraft cabin atmosphere. Of major concern in the third category is

vomit, the aspiration of which is considered particularly prone to occur if an astronaut vomits into the helmet of his space suit. It is pointed out that the hydrochloric acid content of vomit is highly irritative. As well, if food particles are present in the vomit, they can produce primary obstruction of respiratory passages and possibly further chemical irritation. The following discussion deals with the general aspects of chemical inflammation of the lower respiratory passages. Although it is considered possible that some contaminants might be absorbed from the respiratory passages and produce specific toxic effects, such effects can be described only after the hazards and their toxicology have been better defined.

A chemical which enters the lower respiratory tract can induce various respiratory protective reflexes such as coughing, apnea, glottic closure, adduction of the vocal cords and bronchospasm. These reflexes act to exclude the irritant from the deeper respiratory passages, especially the delicate alveolar cells. The stimulating action of an irritant is determined by its cytotoxic nature, by its solubility in water and, of course, by the amount of irritant entering the respiratory passages. Intense stimulation may be effective in temporarily excluding an irritant from, and so minimizing the toxic effects of the irritant in the lower respiratory passages. Unfortunately, however, these reflexes are not so efficient when a large volume of a highly irritating fluid such as vomit is aspirated (20).

After gaining access to the lower respiratory passages, a chemical will produce toxic effects in specific regions of or throughout the passages. This will depend mainly on the amount of the irritant and its physical properties. An irritant gas with a high solubility in water will be extracted by the moist surfaces of the upper respiratory tract and high up in the lower tract, whereas an irritant gas with a low solubility will penetrate deep into the tract producing toxic effects on bronchioles and alveoli. The characteristics of deposition of inhaled particles or droplets in the lower respiratory passages in the weightless environment have been discussed previously. The distance of penetration of an aspirated liquid into the lower respiratory tract will depend mainly on the amount of liquid that enters. An aspirated particle can lodge in various regions of the lower respiratory passages. The more soluble it is, the more immediate and diffuse will be its chemical

action, all other cytotoxic factors being equal.

The inflammation produced by a chemical in the lower respiratory tract is characterized by vasodilatation, congestion and subsequent transudation of plasma through hyperpermeable capillary walls in the involved tissues. This edema fluid distends interstitial tissues and accumulates in the respiratory passages, interfering with the ventilation of the lungs and, if the alveoli are involved, impairs diffusion of respiratory gases across alveolar membranes and perfusion of alveolar capillary beds. Inflammation of the laryngeal and bronchial tissues is usually accompanied by some degree of laryngospasm and bronchospasm, which assist in blocking air flow. Chemical necrosis of tissues may occur, with debris and hemorrhage contributing further to impairment of lung function. Then, as a common and often serious sequel, secondary bacterial infection of damaged lung tissues can occur.

In the light of the above considerations, it is obvious how widely variable the clinical manifestations produced by a chemical irritant in the lower respiratory passages of an astronaut could be. The entry of an irritant into the lower respiratory passages can produce signs and symptoms such as apnea, partial or complete blockage of air entry, stridor, violent coughing, retching, a severe burning or stinging pain in the throat, larynx and trachea, a feeling of substernal pressure, wheezing, dizziness and anxiety. If the larynx is severely involved, laryngospasm and rapidly-occurring interstitial edema of its tissues can seriously compromise air flow, with severe dyspnea, cyanosis and possibly fatal asphyxia coming on within minutes after exposure. Signs and symptoms of acute chemical laryngotracheobronchitis, such as dyspnea, coarse rales and rhonci, cyanosis and the coughing of a copious, possibly blood-stained frothy sputum, can appear over a period of minutes to hours and cause death. Acute chemical pneumonitis usually begins rapidly, either immediately or after a relatively asymptomatic period of up to several hours. If the edema is severe, there is dyspnea and the coughing of a copious frothy sputum which might be blood stained. This edema may lead to cyanosis, right-sided heart failure, "shock" and death <sup>(47)</sup>. Severe necrosis of tissues in the lower respiratory passages can result in fatal hemorrhaging. Surviving

chemical inflammation and damage of one specific or all regions of his lower respiratory passages, an astronaut could develop a secondary bacterial infection over a period of many hours or days. This could manifest as laryngotracheobronchitis, bronchopneumonia, empyema or lung abscess, and could lead to his demise.

The diagnosis of chemical inflammation of the lower respiratory tract is, in most cases, obvious from the history and physical findings alone. It is important to remember that acute pulmonary edema can occur in an asymptomatic individual up to several hours after being exposed to a chemical irritant. If possible on board the spacecraft, chest x-rays could be of some assistance in diagnosing pulmonary edema in its pre-clinical and clinical stages, and secondary complications.

Experimental and apparent clinical success, especially in treating chemical inflammation of the lower respiratory tract due to aspirated vomitus, has been achieved with steroids (4, 11, 20, 22, 31, 32). The exact mode of action of these drugs is unknown (4, 32). Further research is apparently required to definitely establish their effectiveness in treating chemical inflammation in the lower respiratory passages from all causes. The standard method of treatment is the administration of a suitable steroid, such as hydrocortisone sodium succinate, intravenously as soon as possible after an incident. Depending on response to the first dose and the seriousness of the inflammation, repeat doses of such a drug can be given either intravenously or intramuscularly over a period of time. After the acute phase of the inflammation has passed, a suitable oral steroid preparation, such as methylprednisolone, should be taken in decreasing doses for several days.

Other therapeutic measures are taken as dictated by sound clinical judgment. A tracheostomy is a life-saving measure which should be performed as soon as possible in cases with laryngeal edema of rapid onset. It is also effective in cases with severe involvement of the lower respiratory passages, by allowing less obstructed ventilation of the lungs and providing a portal for the removal of copious secretions and possibly blood. Positive pressure oxygen will combat not only hypoxia but also pulmonary edema. Bronchospasm can be relieved with a suitable bronchodilator drug, such as



aminophylline, administered intravenously or intramuscularly. Nebulized isoproterenol might also be used for bronchodilation. Rapid intravenous digitalization will be required in cases with right heart failure, and may be undertaken as a prophylactic measure in potentially serious cases. "Shock" should be treated with a suitable vasopressor, such as metaraminol, administered intravenously. Analgesia and sedation might be indicated. Therapy with a suitable broad spectrum antibiotic might be commenced in serious cases even before manifestations of secondary infection appear.

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## CHAPTER 9

### URINARY CALCULUS

Many authors have postulated that bone will undergo partial reabsorption in the weightless environment (20, 25, 30, 42, 58, 62, 71). They have also pointed out that the resulting excessive excretion of the products of bone reabsorption might be conducive to urinary calculus formation. Accordingly, it is thought necessary to consider urinary calculus a potential medical problem of prolonged space missions until appropriate studies in space prove otherwise. This chapter presents information considered pertinent to the occurrence of urinary calculus in space.

#### Weightlessness and Bone Metabolism

Bone is a living tissue and, like most other tissues in the body, is constantly undergoing the simultaneous processes of formation and destruction (84). In bone formation, a matrix of protein and mucopolysaccharide is first produced by osteoblastic cells. Then calcium and phosphorus, mainly in the form of apatite crystals, is deposited in this matrix. Bone reabsorption is due to osteoclastic cellular activity, which is apparently responsible for the breaking down of both matrix and bone crystals (62). By means of formation and reabsorption processes, bones are remodeled in response to the functional demands which muscular pull, other mechanical stresses, and presumably gravitational forces place on them. This fact was recognized by Julius Wolff in 1868, and has become known as Wolff's law: "Every change in the form and the function of bones, or in their function alone, is followed by certain definite changes in their internal architecture, and equally definite changes in their external conformation . . . . . " (103).

If stresses on bones are sufficiently increased by physical activity, for example, the physicochemical processes of bone formation in the stressed bones will outdistance those of bone reabsorption, and hypertrophic changes will occur. Conversely, if the stresses on bones are decreased to a significant degree, atrophic, or osteoporotic changes will result from reabsorptive processes predominating over formation processes. The osteoporosis

which occurs in an extremity which becomes paralyzed, or is immobilized for a period of time for therapeutic purposes, is a classical example of the effect of decreasing the mechanical stresses on bone.

In accordance with Wolff's law, the state of equilibrium of bone metabolism is influenced by the forces of compression, tension, and shear exerted by weight bearing and muscular activity. One would expect, therefore, that removal of the forces normally exerted by weightbearing, as will occur in the weightless environment, will alter this state in weightbearing bones. Reabsorption processes will exceed formation processes in these bones until bone metabolism, as influenced now by only the forces of muscular activity, returns in time to a state of equilibrium. If the degree of osteoporosis produced by the excessive bone reabsorption is severe and localized, weightbearing bones could become more prone to fracture (20, 84). However, even more important from a space operational standpoint is the possibility that the urinary output of calcium and other products of bone reabsorption could lead to urinary calculus formation, and the extremely incapacitating symptoms therefrom, during a space mission (26, 30, 42, 58, 71, 91, 92).

In various attempts to predict what effect weightlessness will have on bone metabolism, observations made on immobilized patients and healthy experimental subjects have been referred to repeatedly (8, 20, 28, 52, 101, 102, 104). The classical experiment of Deitrick and co-workers (28) illustrates immobilization carried to one extreme. Four healthy young men were immobilized in plaster casts from waist to toes for six to seven weeks. They were placed on constant dietary intakes for several weeks prior to and during immobilization. Pertinent to considerations in this chapter are that immobilization brought about a prompt increase in urinary and fecal calcium excretion, which reached a plateau over a period of four to five weeks. At this time, the urinary calcium output was between two and three times its pre-immobilization level. The serum calcium tended to rise in this study, leading to the suggestion that during immobilization, the increase in calcium excretion and hypercalcemia may actually reflect an increase in bone reabsorption (100). Immobilization also led to an increase in urinary



and fecal phosphorus excretion. The urinary phosphorus excretion began to rise during the first week. It reached a peak which coincided with that of increased nitrogen excretion in the second to third week, decreased somewhat, and then reached a second peak at the sixth to seventh week, when the urinary calcium excretion was at its highest level. Pertinent to considerations of urinary calculus formation is the observation that urine pH rose slightly so that, as will be discussed below, the solubility of calcium phosphate in the urine would have been decreased.

Recently, more practical immobilization experiments have been directed at maintaining recumbent, healthy, young subjects at an optimum level of physical fitness by having them intermittently perform a variety of appropriate exercises (8, 20, 96). Hopefully, such exercises, which will undoubtedly be necessary to compensate for decreases in normal physical activity during space missions, should eliminate the effect of muscular inactivity on bone metabolism. Accordingly, if subjects remain recumbent, the effects of weightlessness on weightbearing bones should be fairly well simulated in these experiments.

Throughout a 30-day bed rest study reported by Brannon and co-workers (20), 18 healthy young subjects performed one of three exercise routines, and six subjects performed no exercise except for being allowed to sit and turn about in bed. All subjects were on constant dietary intakes throughout the study. Since bed rest did not produce an increase in the urinary calcium output in either the exercise or non-exercise groups, the impression was gained that only a small amount of exercise is necessary to preserve muscular integrity and prevent bone reabsorption in a physically fit, normal individual who is confined to bed. Similar studies by Vogt and co-workers (96), in which specific isometric exercises were found to prevent reabsorption of the os calcis, suggests that appropriate exercises might even effectively protect weightbearing bones from reabsorption.

In contrast to the above findings, Birkhead and co-workers (8) failed to prevent bone reabsorption with various exercise regimens in their bed rest study. In this study, eight subjects remained recumbent for 24 days. All had a constant dietary intake during this period. Exercise was performed

on a bicycle ergometer for one hour daily by two subjects in a lying position and two subjects in a sitting position. Four subjects sat in a chair for eight hours daily.

From the studies mentioned above, it is apparent that the relative contributions of muscular activity and the stresses of weightbearing to the maintenance of normal bone integrity still remain undetermined. All exercises which involve the gravity muscles and weightbearing bones simulate weightbearing forces to some degree. For this reason, it is unlikely that the specific effects of weightlessness on the skeletal system will ever be simulated. Whedon <sup>(100)</sup> pointed out that we do not even know the exact manner in which mechanical stresses exert their effects on bone mass. He postulated that these stresses may act through the medium of muscular pull on periosteal surfaces and, in weightbearing, more directly through bone structures and columns, or by combinations of these two and perhaps other factors. On the one hand, muscular pull would seem to be the most important factor maintaining normal bone integrity, since slow rocking in a Sander's oscillating bed was effective in preventing the alteration of calcium balance of normal immobilized subjects <sup>(101)</sup> but not of severe poliomyelitis and paraplegic cases <sup>(104)</sup>. On the other hand, Abramson <sup>(1)</sup> showed that osteoporosis in paraplegics was effectively reduced by weightbearing, hence providing evidence for weightbearing as a factor.

Therefore, it appears that during space missions, efforts should be directed not only at maintaining an optimum level of muscular activity, but also at attempting to simulate the stresses of weightbearing on bone. Carefully selected exercises should prevent loss of muscle integrity, and the bone reabsorption associated with it, in an astronaut who has his physical activity reduced during a space mission. Such exercises, which should maintain stability about weightbearing joints and the fitness of postural musculature, will also contribute to keeping the risk of injuries from mechanical forces in space (Chapter 14) to a minimum. It is thought that an almost if not completely adequate simulation of weightbearing stresses on the musculoskeletal system can be accomplished in space by means of selected exercises and possibly the application of appropriate mechanical forces to the body.

This is an area which certainly requires intensive investigation.

### Urinary Calculus Formation

Although weightbearing forces on the skeletal system might conceivably be adequately simulated in space by various measures, it is believed that at the present time, excretion of the products of bone reabsorption, if only to a minor degree, should be anticipated during prolonged space missions. Since one or more of a number of factors other than bone reabsorption could initiate or enhance the formation of a urinary calculus in an astronaut, they too must be taken into account when considering the prevention of urinary calculus in space. It should be remembered that some of these factors are actually potential side-effects of space operations and, either singly or in various combinations, might be capable of initiating calculus formation even though bone reabsorption might not be occurring.

### Components of a Urinary Calculus

The principle component of a calculus formed in a normal urinary tract in space will probably be basic calcium phosphate principally in the form of either apatite ( $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ ) which is its solid phase about a pH of 6.6, or brushite ( $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ ) which is its solid phase below a pH of 6.6 (33, 34, 36, 77). If a urinary tract is infected with urea-splitting organisms, such as Proteus, Staphylococcus albus and rarely members of the colon group of bacteria, ammonia will be formed. Because of alkalization and ammoniation, a calculus which develops in this case will probably be composed of apatite and calcium magnesium ammonium phosphate; the latter occurs at a pH of 7.1 when the calcium to phosphate ratio in the urine is below the normal mean, and is also known as triple phosphate or struvite (35, 36, 40, 77). It is readily apparent that a calculus consisting of layers of these different crystalline materials can be produced if conditions under which calculi are formed in the urine vary.

The other component of all urinary calculi is organic matrix. It is apparently composed of constant amounts of mucoprotein and mucopolysaccharide, and is evenly distributed throughout a calculus <sup>(19)</sup>. As will be pointed out below, the role of matrix in calculus formation has received

much debate in the past few years.

### Basic Mechanisms of Urinary Calculus Formation

The mechanisms underlying the formation of a urinary calculus remain essentially undefined. Current thought in this area has been reviewed by Boyce and King <sup>(17)</sup>, Howard <sup>(51)</sup>, Holt <sup>(50)</sup>, Flocks and Bush <sup>(40)</sup>, Fleisch <sup>(39)</sup>, and many others <sup>(10, 41, 43, 69, 72, 77, 89)</sup>.

Many investigators in this area have held the view that organic matrix is required as a framework for calculus formation, while crystal deposition appears to be a secondary phenomenon. Evidence for this was given by the observation that even though concretions of matrix material with little inorganic salt content do occur, the converse is not true <sup>(12, 17)</sup>. Fleisch <sup>(39)</sup> pointed out that if no matrix is formed, no calculus can build up, the maximum mineral deposit then being well known "urinary sand".

Boyce and co-workers <sup>(17, 18, 19)</sup> have suggested that the matrix is formed from the aggregation and molecular reorientation of uromucoid, a mucoprotein-mucopolysaccharide conjugate. Uromucoid is the largest single component of the normally excreted urinary bicolloids, and notably is one of the bicolloids which is markedly increased in patients with urinary calculus disease <sup>(14, 15, 16)</sup>. In a normal state, it is believed that there is some binding of calcium and phosphorus by uromucoid molecules, but little tendency for the molecules to aggregate <sup>(17)</sup>. Accordingly, some factor would have to alter the binding capacity of uromucoid molecules, so permitting molecular aggregation and orientation to form the structural characteristics of the calculus matrix <sup>(17)</sup>. The oriented molecules would then act as templates or epitactic stimuli for apatite or other crystal formation depending on chemical conditions in the urine <sup>(17)</sup>.

The origin of uromucoid remains unknown, however. Because of the high molecular weight of its constituents, Boyce and King <sup>(17)</sup> have suggested that it is of urinary epithelial origin, either from the renal tubules or the transitional epithelium. The hypothesis that the mucoprotein and mucopolysaccharide moieties from the reabsorption of bone matrix are excreted in the urine and reform under the proper ambient conditions in the urine

into uromucoid or a similar substance remains to be substantiated (50, 87). This mechanism could explain the origin of the matrix in urinary calculi attributed to excessive bone reabsorption. Comparison of the urinary calcium excretion rates of idiopathic calculus formers with healthy non-calculus forming individuals has indicated that under all dietary regimens employed, 24-hour calcium excretions of stone formers exceeded that of controls (13, 17, 60, 64, 88). Accordingly it has been suggested that hypercalciuria per se should be considered a possible stimulus leading to the increased production of uromucoid (14, 40). It is of interest to note that some of the calculus-formers whose urinary calcium excretion was reduced by diet still formed stones. These stones were described as non-opaque, pure matrix-material stones which contained no calcium.

How hypercalciuria might stimulate the production of uromucoid in the urinary tract is a question to be answered. To confuse the issue, it has been repeatedly pointed out that prolonged hypercalciuria is not always associated with urinary calculus formation (2, 49, 67, 69, 77). Boyce and Garvey (12) found evidence that an organic matrix may form if the urinary tract epithelium is irritated by precipitated crystalloids. This possible irritative mechanism might also explain the origin of the matrix in the calculi which have been attributed primarily to infection of the urinary tract. In the case of infection, the bacterial and epithelial debris produced by the infection might actually act as the nuclei initiating stone formation (40).

Finally, it has been postulated that uromucoid might be excreted by the kidneys as the result of abnormalities, which have apparently been seen histologically in the renal connective tissue matrix (3). The possibility that increased calcium transport through the kidneys might produce histologic changes has doubtlessly been considered. A possible relationship between uromucoid production and physiological "stress" has been suggested (4).

Research has, however, led other investigators to believe that organic matrix is not a crucial element for urinary calculus formation, but rather an incidental inclusion in calculi. In a number of experiments, Vermeulen and co-workers (61, 93, 94) have induced the crystalline deposition of

calculus minerals on a wire loop placed in a great variety of modified urine media. Their artificial calculi often assumed many of the structural characteristics of authentic calculi. This was found to depend on the curious phenomenon of "habit modification", or the influence which other constituents of the urine had on the growth and reworking of the calcium phosphate crystalline mass. Surprisingly, the artificial calculi also contained a matrix-like component. Their experiments also demonstrated that the matrix arises by incorporation of non-dializable urinary constituents into the developing concretion, for when a medium of urine ultrafiltrate was used in place of whole urine, no such matrix component was present. These observations were interpreted as evidence that urinary calculus formation is a crystallization phenomenon and that organic matrix is a nonessential component resulting from protein adsorption onto crystalline surfaces, an occurrence well known to crystallographers. It was suggested that matrix may, however, act by modifying crystal habit and also serve as a barrier to dissolution of a developing calculus.

An adequate explanation for the initiation of urinary calculus formation has also not been given. It has been suggested that the stimulation of uromucoid agglomeration and molecular orientation might depend on the presence of a suitable nidus, or nucleus, such as an agglomeration of calcium phosphate crystals, desquamated urinary tract epithelium, bacteria, or some mixtures of these entities (12, 40, 87). The hypothesis that urinary calculi can originate as microscopic calcific deposits in the renal parenchyma is supported by animal experimentation and the finding of such deposits, especially in patients with hypercalciuria and proven urinary calculus formation (2, 22, 78, 93). Animal experiments have also indicated the possible significance of an inadequate dietary intake of vitamin A in producing keratinization and excessive desquamation of urinary epithelium, which can then serve as a nidus for calculus formation (25, 32, 40, 46). This might explain the unusually high incidence of urinary calculus disease in the citrus areas of Florida and California, for citrus fruits are

high in alkaline ash, and low in protein and vitamin A (41).

### Factors Influencing Urinary Calculus Formation

Since the mechanisms underlying the formation of a urinary calculus are not understood, the reasons for the known or postulated effectiveness of the various preventive measures to be discussed below can often not be adequately explained. The use of such measures has been derived from the recognition of the many factors which influence urinary calculus formation. Pertinent to considerations of urinary calculus formation in space are various factors concerned with the urinary output of the products of bone reabsorption, the solubility of calculus crystalloids in the urine, the excretion of uromucoid in the urine, the solubility of uromucoid in the urine, and the deposition of crystalloids in the calculus matrix. Other factors which bear mentioning are urine stasis and foreign bodies. It will become apparent that many of these factors can be implicated in more than one way in urinary calculus formation.

The high incidence of urinary calculus formation associated with recumbency is well documented (40, 53, 59, 76). It must be pointed out, however, that urologists generally attribute this to some renal complication attendant on recumbency, such as urinary infection, a congenital anomaly of the drainage system or perhaps drug-induced injury of the kidney (11). The authors quoted above were unable to differentiate clearly between urinary tract infection, and no attempt was made to look into the use of potentially nephrotoxic drugs, such as streptomycin, which were administered to a number of the patients studied (11). Presumably, an excessive excretion of reabsorbed calcium and phosphate, and possibly bone matrix breakdown products, could still initiate and support calculus growth in the normal urinary tract of a recumbent individual. Any contribution which urine stasis and sedimentation of precipitates makes to the formation of a urinary calculus in a recumbent individual would, of course, not occur in space. However, although it must for the present be assumed that excessive bone reabsorption associated with weightlessness will be conducive to urinary calculus formation, the above and other considerations in this

chapter indicate that in the absence of other contributing factors, the risk of urinary calculus disease from bone reabsorption per se in space will be extremely low.

Disorders which cause excess urinary calcium excretion must be taken into consideration here, for they would probably enhance any calculus-forming tendency predicted for the weightless state. Particular emphasis is placed on screening out potential astronauts who have idiopathic hypercalciuria.

Dietary factors which affect the amount of calcium excreted in the urine must be considered. There is no evidence that a high oral calcium intake has any significant effect on the urinary calcium of normal human beings <sup>(17)</sup>. On the other hand, it appears that in order to produce a significant lowering of the urinary calcium output, dietary and even therapeutic measures would have to be so rigorous that they would be impractical in space <sup>(17, 50, 65)</sup>. The fact that the intestinal absorption of calcium and the amount of it subsequently excreted in the urine is directly influenced by the dietary level of vitamin D should be remembered in selecting the diet of an astronaut <sup>(17)</sup>. It might also be necessary to take into account the amount of vitamin D production in the astronaut due to his contact with ultraviolet light in his space environment. Interestingly, animal experiments have shown that vitamin A will counteract the hypercalciuric effects of hypervitaminosis D, so that an optimum level of vitamin A in the diet of an astronaut should also be assured <sup>(24)</sup>.

The urine of normal people is often, although not always, supersaturated to a minor degree with calculus-forming salts. Various factors, such as ion concentration, pH, complexors, solubilizers and crystallization inhibitors, fortunately make degrees of supersaturation in urine much more than if these salts were dissolved in water <sup>(39)</sup>. Precipitation probably does not occur due to the fact that the ion concentration required to start forming first crystals is much higher than the concentration necessary for already existing crystals to grow further <sup>(39)</sup>.

The concentrating effect of a low urine output tends to promote crystallization <sup>(36)</sup>. Inadequate fluid intake, and hence an inadequate urine



production, has been implicated as a cause of the seemingly high incidence of urinary calculi in individuals exposed to high environmental temperatures during the summer months (21, 75). The high incidence of urinary calculus observed in flying personnel has also been attributed to dehydration, exposure to high environmental temperatures and voluntary restricted fluid intake (55). However, this conclusion may be invalid since the study and control populations were, respectively, high and low incidence groups by virtue of their ages (50).

It has been well demonstrated that the pH of the urine is an important factor affecting crystallization (33, 36, 69, 77, 82). From in vitro studies of the various factors which influence the solubility of calcium phosphate, Elliot and co-workers (33, 36) concluded that average urine specimens which have a pH consistently over 6.6 will be saturated with calcium unless the urinary calcium output is less than 50 mg per 24 hours. This calcium output value is approximately one-quarter to one-third of the 24-hour output value of normal individuals (13). Based on similar studies by Meyer (68), it has been stated that calcium phosphate will remain dissolved only as long as the pH of the urine is 5.6 or lower (87). This "critical" pH corresponds to maximum average 24 hour urinary calcium output values of approximately 525 and 825 mg (assuming a 24 hour urinary output of 1500 ml) in the two urine specimens studied by Elliot and co-workers (36). Moreover, for normal urine volumes, this solubility-pH relationship of calcium phosphate is such that at a pH of 6, the calcium phosphate of the urine is at least two times, and at a pH of 7, eight times supersaturated. The contributions to calculus formation of a diet-induced alkalinization of the urine and of infections of the urinary tract by urea-splitting organisms which alkalinize the urine are readily apparent, the latter having been well substantiated clinically (32, 40, 77).

Since urine is normally often supersaturated with calculus-forming crystalloids, numerous investigators have searched for excreted substances which could be responsible for keeping these calculus-forming salts in solution. Butt (21) suggested that protective colloids are present in the urine, and that some derangement in these colloids was responsible for calculus formation. His hypothesis has not been proven, however (16, 37, 95).

A great deal of interest has been focused on the possible solubilizing role of citric acid in the urine. Citric acid chelates, or binds calcium ions to form a soluble complex <sup>(44)</sup>. The high incidence of urinary calculi in patients being administered the carbonic anhydrase inhibiting drug, acetazolamide, has been attributed to a concomitant decrease in the concentration of citric acid in the urine <sup>(63)</sup>. However, it is pointed out that the concentrations of many other substances in the urine change on administration of this drug. The low urinary citric acid levels which have been found in patients who are chronic calculus formers have been attributed to impaired renal function or the utilization of citric acid by organisms infecting the urinary tract secondary to the calculus disease <sup>(26, 48, 54, 64, 69, 85)</sup>. Experiments indicate that urinary citric acid excretion fails to be increased by a diet-induced increase in urinary calcium excretion <sup>(64)</sup>. Thus, even if urinary citric acid is important in preventing calculus formation, a possible increase in its excretion to compensate for a urinary hyperexcretion of calcium would appear to be inadequate. If a therapeutic increase in urinary citric acid excretion is contemplated, it is important to note that ingested citric acid (1.5 to 2.5 percent of ingested citric acid given in doses of 2 to 20 gm) has little if any effect on the level of citric acid in the urine <sup>(56, 83)</sup>. Moreover, even though food and ingested alkalis such as sodium bicarbonate increase urinary citric acid excretion, they would not be useful since the resulting alkalization of the urine would markedly decrease the solubility of the calculus crystalloids in the urine <sup>(9, 64, 105)</sup>. Finally, it is noted that recent evidence suggests that citrate may play a less important part in maintaining certain salts in solution than has been thought hitherto <sup>(21, 95, 106)</sup>.

As mentioned previously, factors concerned with the excretion of a calculus matrix-forming substance in the urine are inadequately defined. It has been suggested that the matrix might form from the excreted mucopolysaccharide and mucoprotein products of bone reabsorption, or mainly from uromucoid, the increased production of which might be stimulated by hypercalciuria per se, by irritation of the urinary tract by precipitated

crystalloids or infection of the urinary tract, by pathological abnormalities in the renal connective tissue, or by physiological "stress" (3, 4, 12, 40, 51, 87). The only therapeutic measure directed specifically at the production of matrix material was justified by the finding that increased amounts of uromucoid are released in the urine due to a disorder in the renal connective tissue (3, 17). Anti-inflammatory agents, such as aspirin, corticosteroids, corticotropin, and phenylbutazone, were given to chronic calculus-forming patients. The potential usefulness of such a measure has not been established, however. Moreover, there is no evidence that such a connective tissue change, which could be treated with such drugs, accompanies hypercalciuria in "normal individuals".

The factors which affect the solubility of uromucoid in the urine also remain undefined. Undoubtedly the urine volume produced will influence the solubility of uromucoid as well as crystalline calculus components.

Intense interest has been focused recently on factors which appear to influence the deposition of crystalloids in the calculus matrix. Based on the fact that bone and renal calculi both consist of crystalline and matrix phases, it has been speculated that the identification of urine constituents which affect crystal deposition in bone might afford added insight into the genesis and growth of calculi within the urinary tract (89). Despite the presence of similar calcium and phosphorus concentrations in urine specimens, it has been found that the urine from most patients with renal calculus disease mineralizes, in vitro, a test substance of hypertrophic bone cartilage from rachitic rats, whereas urine from most normal subjects does not (51, 70, 89, 90). Studies designed to identify constituents which might account for this lack of matrix mineralization by urines of "normal" individuals have demonstrated that there are a variety of dialysable substances in the urine which, if present in adequate concentrations, will prevent the mineralization of rachitic cartilage (7, 51, 70, 89). Although it is thought likely that there are as yet unidentified urine substances which are of importance in determining mineralizing propensity, the inhibiting effects of trace metals such as zinc, manganese, cadmium, cobalt, chromium, and vanadium have been proven (6, 7, 89). The most

potent of these inhibitors are zinc and manganese (89). Magnesium has been found to enhance the inhibitory effect of the trace metals and also alone, in a sufficient concentration, to be inhibitory (70, 89). It is thought that these elements inhibit mineralization by blocking matrix or crystal templates which are necessary for calcium phosphate crystal formation (6, 39, 89).

Possibly acting in a similar fashion to the trace metals, pyrophosphate has been found to inhibit mineralization of rachitic cartilage and to markedly increase the solubility of calcium phosphate in solution (39, 89). It has been demonstrated that urinary pyrophosphate is diminished in many patients who are chronic calculus formers (39). To test the possible therapeutic benefits which might be derived by increasing the concentration of this compound in the urine, several investigators have been administering oral sodium or potassium orthophosphate, which is excreted in the urine as pyrophosphate, to chronic calculus-forming patients (6, 51, 79, 89). This effect is apparently accompanied by a fall in calcium excretion and an increase in citrate excretion, both of which might also be expected to reduce the tendency for stone formation to occur (79). Although there is insufficient confirmatory data at the present, the results of such treatment have reportedly been encouraging, for apparently no patient given orthophosphate sufficient to ensure consistent excretion of a non-mineralizing urine has formed new urinary calculi or has increased the size of pre-existing calculi. The effect of pyrophosphate on the urinary pH which, as previously stated, exerts a profound effect on calcium phosphate solubility has not been stated (6).

It has not been postulated whether pyrophosphate or the trace metals mentioned above could play a role in preventing uromucoid agglomeration to form the matrix of a urinary calculus. Further research in this area will, no doubt, give added insight into the mechanisms involved in urinary calculus formation, and possibly substantiate the effective clinical usage of other non-toxic inhibitors. Such research is certainly pertinent to considerations of the possible requirements for therapeutic measures directed at the prevention of urinary calculus in space. Since there is now good experimental evidence that chronic calculus-forming patients, and possibly even individuals

with a calculus-forming tendency have an absence of factors concerned with protection from matrix mineralization, a test of astronaut candidate urines for mineralizing propensity might be considered, if only for experimental purposes.

Other factors which influence urinary calculus formation and should be mentioned here are urinary stasis and the presence of foreign bodies in the urinary tract. It is thought that urinary stasis promotes the precipitation of calculus crystalloids by allowing crystalloid concentrations in certain portions of the renal collecting system to rise above critical levels <sup>(40)</sup>. Sedimentation of precipitates in various parts of a normal urinary tract should not occur in a weightless environment, however, so that weightlessness would counteract this calculus forming effect of urinary stasis. The well known fact that static urine is more likely to become infected is another complicating factor. Although originally thought otherwise, operational experience in space is proving that another cause of urinary stasis - change in the sensation of urgency - is not a problem in the weightless environment <sup>(97)</sup>. It is probable that earlier reported difficulties in voiding in the weightless environment were psychogenic in origin, due primarily to the demand placed on subjects, relatively unfamiliar with the sensations of weightlessness, to initiate micturition within a short period of time in a small aircraft cabin.

Foreign bodies in the urinary tract, such as a urinary catheter, apparently stimulate urinary calculus formation not only by acting as a nidus for crystalloid deposition but also by promoting infection of the urinary tract <sup>(40)</sup>.

### Clinical Manifestations

The optimum use of measures directed at adequately controlling the various factors which could be responsible for urinary calculus formation in space would minimize not only the likelihood of urinary calculus in space, but also the rate at which a once initiated urinary calculus grows. As a result, the clinical manifestations of a urinary calculus might appear after an astronaut has been exposed to the weightless environment for many months

or even years.

Some indication of the time required for a urinary calculus to form and grow to a size which results in clinical manifestations can be derived from studies which have noted the date of immobilization and the date of appearance of signs and symptoms of urinary calculus in patients immobilized for prolonged periods of time due to orthopedic injuries. In one study, 15 out of 800 such patients developed urinary calculi <sup>(53)</sup>. The shortest duration for the appearance of symptoms was 74 days, the longest 1200 days, and the average 362 days. A similar study reported a shortest duration of 76 days, a longest of 622 days, and an average of 276 days <sup>(38)</sup>. In reviewing this data, it is important to note that the conditions under which calculi form in patients do not simulate conditions in space for, as pointed out above, urologists generally attribute calculus formation in recumbent patients to some renal complication attendant on recumbency, such as urinary infection, a congenital anomaly of the drainage system or perhaps drug-induced injury of the kidney. Furthermore, a calculus of a size which is sufficient to produce clinical manifestations may be present in the urinary tract for days to months, or even years before becoming clinically evident.

The major clinical manifestations produced by a urinary calculus are the pain which the calculus causes as it passes down a ureter, the secondary changes brought about by the irritation of the urinary tract by the calculus, and the manifestations associated with accompanying infection <sup>(40, 47, 82)</sup>.

Pain is usually associated with the passage of the calculus down the ureter. It is classically described as intermittent or colic (so-called ureteral colic), excruciating and agonizing, and is usually prostrating. Each attack of colic lasts a few minutes, and after a variable period of usually a few minutes, is repeated. Quite often, however, the pain produced by a urinary calculus is quite insidious, depending on the size, shape and position of the calculus. Occasionally, it might imitate other abdominal conditions, such as appendicitis. A calculus in the renal collecting system is frequently clinically silent for a prolonged period of time. Once in the

kidney pelvis, however, it usually produces almost immediate symptoms, particularly if it is of such a size to act as a proverbial ball in a funnel, blocking drainage from the kidney <sup>(99)</sup>.

Ureteral colic is due either to distension and hyperactive peristaltic waves resulting from an obstructing calculus, or to vasospasm in the ureteral wall adjacent to the jagged surface of the calculus <sup>(57)</sup>. It is not really perceived as being along the course of the ureter, but in regions supplied by spinal segments T<sub>11</sub>, T<sub>12</sub>, L<sub>1</sub> and L<sub>2</sub> (ilioinguinal, iliohypogastric and genitofemoral nerves) <sup>(57)</sup>. Depending on the location of the calculus in the ureter, this "referred pain" may then arise in the costovertebral angle on the involved side and radiate around the loin anteriorly and caudally to the respective inguinal or medial thigh regions and testis, or even down into the penis. Ureteral colic often begins and is most severe in the costovertebral angle and flank and moves downwards as the calculus passes the ureter.

If muscular spasm accompanies ureteral colic, the muscles supplied by the spinal segments (T<sub>11</sub> to L<sub>2</sub>) will be involved <sup>(46)</sup>. These muscles include the lower portions of the external abdominal oblique, internal abdominal oblique, and transverse abdominal muscles and the cremaster muscles <sup>(57)</sup>. Nausea, vomiting, profuse perspiration and syncope may accompany severe ureteral colic <sup>(82)</sup>. Between attacks of colic, afflicted individuals often complain of soreness and tenderness, particularly in the renal and lower anterior abdominal areas <sup>(82)</sup>.

The most frequently observed secondary changes brought about by the irritation of the urinary tract by a calculus are hematuria and dysuria. Hematuria is common, resulting from contact of a calculus with the lining of the ureter. Red blood cells can be found, intermittently or continuously, in the urine of persons with a urinary tract calculus.

Dysuria, or painful urination can be caused by reflex reaction in the bladder due to ureteral activity from a calculus in the terminal ureter by the calculus irritating the bladder wall, or by secondary infection <sup>(47)</sup>.

Longstanding ureteral obstruction often leads to infection above the site of obstruction. The symptoms and signs are those of pyelonephritis, which

is characterized by chills and fever and other systemic toxic manifestations, loin and costovertebral angle aching and tenderness and renal enlargement on the affected side, and pyuria. A low grade infection often persists after an acute attack subsides, especially if a partially-obstructing calculus is present. Such an infection can be extremely debilitating <sup>(47)</sup>.

### Diagnosis

An afflicted astronaut's history and physical examination should yield the characteristic clinical findings outlined above. If his urine can be examined in space during a period of ureteral colic, blood will probably be found, if not masked by infection. It is important to note that red blood cells may be present in the urine in the absence of or for some time prior to the onset of symptoms of calculus. This gives good reason for serial urine analyses if a urinary calculus is suspected.

Almost all symptomatic urinary calculi should be visualized by simple x-ray techniques, if possible in space <sup>(47)</sup>. X-rays of the abdomen, including the urinary tract, prior to missions in space will assist in distinguishing a calculus from other abdominal calcium-containing structures, such as phleboliths and calcified mesenteric lymph nodes, as well as ruling out the existence of a urinary calculus. If ever possible in space, intravenous pyelography could be of great value in confirming the location of densities seen on the plain film, and in assessing the degree of urinary obstruction.

### Prevention

The various factors which could influence the formation of a urinary calculus in space have been discussed previously. It is at these factors that optimum non-therapeutic and possibly various therapeutic measures must be directed. It is assumed that appropriate investigative procedures in astronaut candidates will rule out any tendency to urinary calculus formation. The fact that urinary calculus disease has a familial incidence should be kept in mind while taking a candidate's medical history. A normal urinary tract must be ensured by searching for congenital anomalies and infection of the urinary tract, and by assuring that there is no difficulty voiding or a



calculus already present in the urinary tract. Calcium metabolism must be studied intensively, especially with serum calcium and phosphorus determinations, and measurements of 24 hour urinary calcium output while the dietary calcium intake is controlled. As pointed out above, testing of the mineralizing propensity of the urine might be found feasible in all or certain cases in the future.

Hopefully, future studies will determine to what extent the intermittent use of selected exercises and other measures in space will simulate normal weightbearing stresses on the skeletal system. At the present time, it appears that the most appropriate exercises which an astronaut can undertake in space are of the isometric or dynamic tension type. It is assumed that an astronaut will be in optimal physical condition prior to a mission in space and that such exercises will maintain this level of physical condition, and hence prevent reabsorption of bone at least from reduced muscular activity in space. One question which requires answering by research is whether an individual with a higher than average urinary calcium output would have a greater than normal urine calcium excretion when immobilized or placed in a weightless environment <sup>(6)</sup>.

To produce a significant lowering of a urinary calcium output by restricting an astronaut's dietary calcium intake, dietary measures would have to be so rigorous that they would be impractical. Since the dietary level of vitamin D directly influences the intestinal absorption of calcium, the daily intake of this vitamin in the diet should not exceed normal recommended values. It might also be necessary to restrict the amount of vitamin D production in an astronaut by controlling his exposure to ultraviolet light.

The urinary output should be maintained continuously at a reasonable level with an adequate oral fluid intake. A urinary output of at least 2000 ml per 24 hours has been recommended <sup>(87)</sup>. This would require a daily fluid intake of at least 3000 ml per 24 hours or more, depending on body fluid losses from other causes, such as perspiration <sup>(25, 87)</sup>.

In order to maintain the urinary pH at as low a level as possible in space, the dietary intake of urine-alkalinizing foods should be kept to a minimum and urine-acidifying foods to a maximum, while still maintaining

adequate nutrition and food palatability. The rigorous treatment of urinary tract infections, which are usually caused by urine-alkalinizing organisms, is emphasized.

The role of citric acid in maintaining calculus salts in solution is controversial. It is again pointed out that even though certain alkaline foods increase urinary citric acid excretion, their tendency to alkalinize the urine would have a detrimental effect on the solubility of the calculus crystalloids, so contraindicating their use in an astronaut's diet.

At the present time, there appears to be no non-therapeutic measures which can be directed at inhibiting the excretion of calculus matrix-forming substances in the urine, other than the measures directed at preventing bone reabsorption in the weightless environment.

The maintenance of the urinary output at a reasonable level will help to maintain uromucoid in solution. It is pointed out that an adequate dietary intake of vitamin A must be assured to prevent the formation of the calculus nidus presumably made up of cells which are desquamated from the lining of the urinary tract secondary to a deficiency of this vitamin (87).

Further studies identifying constituents in the urine which might inhibit the deposition of crystalloids in the calculus matrix might give reason for increasing these constituents in the diet. As mentioned previously, an increased urinary concentration of trace metals, such as zinc and manganese, may not only decrease the mineralizing propensity of the urine but also inhibit calculus formation. Magnesium apparently enhances the inhibitory effect of the trace metals. These metals are non-toxic when ingested in the amounts considered as possibly being adequate for prevention of calculus formation (44).

Urinary voiding should be scheduled if there is any possibility of a diminution in the sensation of urgency in space, so minimizing the possibility of urinary stasis contributing to calculus formation. It is noted that if a urinal sealed to the skin is to be used in space, this apparatus should not produce an elevation of intravesical pressure above that required for normal micturition on earth in order to accomplish a complete voiding, which should leave a residual urine of less than 12 ml (31).

The use of an indwelling catheter should be avoided if possible in space.

If an indwelling or any other form of catheterization is required, however, an appropriate bacteriostatic agent, such as sulfadimethoxine, should be administered for a suitable duration to prevent secondary infection. If an indwelling catheter is used, the bladder should be irrigated with an appropriate solution, such as normal saline, and the catheter replaced periodically.

Since most therapeutic measures produce disagreeable side-effects, their use is indicated only if it appears that the non-therapeutic measures mentioned above could possibly fail to provide adequate protection of an astronaut from urinary calculus in space. One or more therapeutic measures might be attempted.

In the future, it might be possible to administer drugs which have an inhibiting effect on the bone reabsorption due to weightlessness. The drugs of current interest in this respect are derivatives of gonadal hormones (74, 100, 102). It is noted that hormonal side-effects might be a problem with prolonged usage of such agents. Further research in this area is indicated, however.

Orally administered sodium phytate diminishes calcium absorption in the intestine by forming an insoluble complex with calcium in the intestinal lumen (40, 45, 87). Cellulose phosphate has also been found to exert the same effect (29). If the dosages of these compounds are adequate and the dietary calcium intake is minimized, it is conceivable that the hypercalciuria resulting from bone reabsorption in space could be effectively controlled. However, their use in space might be contraindicated because they have a tendency to produce a painless diarrhea (87). Moreover, these compounds, especially phytate, increase the urinary phosphorus excretion, with the result that a favorable situation for calculus formation could possibly occur under certain conditions (29, 87).

Just as a decrease in the urinary excretion of calcium diminishes the formation of calcium-containing calculi, so also a decrease in the excretion of phosphate diminishes the formation of calcium phosphate calculi (87). Shorr devised a low phosphate diet supplemented by aluminum-containing drugs in the form of either basic aluminum carbonate gel or aluminum

hydroxide gel. The aluminum impairs phosphate absorption in the intestine by forming the insoluble compound, aluminum phosphate, in the intestinal lumen. The Shorr regimen has been highly effective in the prophylactic treatment of chronic calculus formers (65, 66, 86, 87). It might even be effective in maintaining a non-precipitating level of calcium phosphate in the urine in space, if excessive bone reabsorption should occur. However, the gel is constipating, and the diet tasteless and also constipating (65, 87). Accordingly, the prolonged use of the Shorr regimen in space is not recommended.

Different orally administered substances have been used to increase the acidity of the urine, especially ammonium chloride, ammonium nitrate and sodium acid phosphate (23, 27, 87). Menthenamine mandelate is currently being favored by most urologists and might be considered as being appropriate for use in space if acidification of the urine by drugs is indicated (73). This drug also acts as a urinary antiseptic, and so could also reduce or eliminate the contribution of a urinary tract infection to stone formation (5). It is almost without side-effects in contrast to the other drugs mentioned above (5).

Even if increased levels of urinary citric acid might have a solubilizing effect on urinary crystalloids, it must be remembered that ingested citric acid has little if any predictable effect on the level of citric acid in the urine. Moreover, even though ingested alkalis such as sodium bicarbonate increase urinary citric acid excretion, their tendency to alkalinize the urine would have a detrimental effect on the solubility of calculus crystalloids, so contraindicating their use.

The importance of adequately treating any infection in the urinary tract in space cannot be overemphasized. The marked influence which such an infection can have on stone formation, especially if the infection is caused by urea-splitting organisms, is well known.

The possibility of orally administered trace and other metals effectively preventing urinary calculus formation has been mentioned above. These metals would undoubtedly be administered in small quantities, and so could be added to the food. The toxicology of such metals should be thoroughly assessed before such a measure could be considered, however.

The encouraging results with orally administered orthophosphate in inhibiting calculus formation in chronic calculus-forming patients may prove this agent worthwhile for use in preventing urinary calculus in space. In "therapeutic" doses, the drug has apparently no side-effects other than occasionally producing diarrhea <sup>(6)</sup>.

### Treatment

In the foreseeable future, a urinary calculus which causes signs and symptoms in space will have to be managed conservatively either until it is passed spontaneously or until manipulative or surgical removal of it can be attempted back on Earth. Fortunately, upwards about 80 percent of all urinary calculi are passed spontaneously <sup>(80, 81, 98)</sup>.

Ureteral colic, irrespective of type of stimulus causing it, can be alleviated to some degree by morphine, meperidine, or other central nervous system analgesic drugs <sup>(57)</sup>. If the colic is primarily due to vasospasm, its prompt relief might be achieved with the use of vasodilating drugs, which act either directly upon blood vessels (e.g., sodium nitrite and papaverine) or by blocking transmission of nerve impulses through sympathetic ganglia (e.g., a tetraethylammonium compound) <sup>(57)</sup>.

An adequate urinary output in an astronaut suffering from urinary calculus should be maintained by forcing his oral intake of fluids or, if necessary, by giving him fluids intravenously. A urine output of at least 3000 ml per 24 hours should be assured.

A urinary bacteriostatic agent, such as sulfadimethoxine, should be administered to an astronaut from the time that clinical manifestations of a urinary calculus appear. An infection might still develop above a partially or completely obstructed site in a ureter, in which case the administration of a suitable antimicrobial, such as nitrofurantoin or chloramphenicol, is indicated.

A sedative, such as sodium phenobarbital might be required. Active movement of the astronaut should be encouraged, however.

There appear to be no orally or parenterally administered agents which are effective in dissolving a urinary calculus <sup>(87)</sup>.

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## CHAPTER 10

### MEDICAL IMPLICATIONS OF CARDIOVASCULAR ADAPTATIONS TO WEIGHTLESSNESS

Even during prolonged space missions, optimum physical fitness, and hence the capacity of the cardiovascular system to respond adequately to a given work load in space, should be maintained by the combined effects of routine physical activity and an appropriate exercise regimen. It is generally thought, however, that certain cardiovascular adaptations to the weightless space environment will still occur. The question arises as to whether such adaptations could affect the likelihood of occurrence or severity of medical problems arising from certain hazards of space operations, especially if a medical problem should occur in the period immediately after an astronaut returns to a gravity environment.

In this chapter the literature is examined in an attempt to determine what cardiovascular adaptations to weightlessness do occur, the medical implications of these adaptations, and finally the appropriate measures which can be taken to prevent adverse effects of these adaptations on astronauts. This is not an exhaustive review of the physiology of weightlessness. Further information on more specific aspects of this area can be obtained from a number of recent reviews which will be cited.

#### Cardiovascular Adaptations

At the present time, cardiovascular adaptations to weightlessness can only be inferred from data obtained in a great number of ground-based experiments which were intended to simulate the effects of weightlessness on the cardiovascular system, and from in-flight and post-flight observations made on those astronauts who have been exposed to weightlessness for up to a few days in duration. By means of bed rest and water immersion, ground-based experiments have attempted to minimize the effect of intravascular hydrostatic pressures due to the force of gravity. Most of the work in this area has been conducted by Birkhead and co-workers<sup>(14, 16)</sup>, Graveline and co-workers<sup>(46, 49, 50)</sup>, Miller, Stevens and co-workers<sup>(75,</sup>

77, 78, 79, 94, 97), Vogt, Vallbona and co-workers (107, 111, 116, 117, 118, 119, 121) and others (69, 99). This area has been reviewed by Lamb (59, 60, 61), McCally and Graveline (71) and others (1, 43, 50, 70, 108, 128). The extrapolation to operational space conditions of cardiovascular findings in individuals exposed to prolonged bed rest or complete water immersion must be guarded, however, for these conditions do not completely eliminate the effects of gravity on the cardiovascular system. Moreover, even though physical and cardiovascular "fitness" has been maintained under such conditions with periodic exercises, the type and degree of routine physical activity, and in turn the cardiovascular dynamics of astronauts in the spacious cabins of spacecraft to be used for prolonged missions has not been, and probably can not be, simulated.

Most observations of cardiovascular responses of astronauts exposed to weightlessness have been made in the immediate post-flight period. Cardiovascular data for all American missions (up to 14 days) and Russian missions (up to 5 days) have been reported (8, 12, 39, 83, 87, 88, 91). Findings must again be viewed with caution. Restriction, limited physical activity during missions, and post-flight fatigue are factors which have effects on the cardiovascular system similar to those which have been predicted for weightlessness. Post-flight data might on occasion have also reflected the effects of dehydration, and physiologic events which might be associated with the vague feeling of "let-down" often experienced after a prolonged emotionally and physically stressful event.

During up to 42 days of bed rest, 7 days of complete water immersion and 14 days of weightlessness, recordings of systolic and diastolic pressures, pulse-rate, heart sounds, and electrical activity of the heart have remained within normal limits, even in the face of marked physical inactivity which led to diminished exercise tolerance (8, 12, 14, 28, 49, 50, 75, 77, 79, 83, 87, 88, 97, 107, 118). Therefore it appears likely that prolonged weightlessness should not alter cardiac function if cardiac work capacity is maintained. This is consistent with the conclusion drawn from application of sound biophysical principles to the circulation,



in that the hydrostatic factor ( $\rho gh$ ) does not affect the driving forces of the circulation directly and inertial factors in the circulation would not be affected at all by weightlessness (24, 71).

It is generally believed that a cardiovascular adaptation to prolonged weightlessness is lowering of blood volume, with decreases of both the plasma and red cell fractions of the blood. In conditions of bed rest and complete water immersion, healthy subjects have consistently demonstrated an acute fall in plasma volume, accompanied by a diuresis and a loss of weight (28, 49, 50, 61, 69, 75, 77, 79, 85, 94, 97, 119, 120, 121). Most of this initial contraction of blood volume has occurred during the first 24 to 48 hours of exposure to these conditions (61). The maximum decrease in plasma volume observed has usually been in the range of 500 ml, or about 10 percent of the body weight (49, 75, 77, 80, 94, 97). Although decrease in blood plasma leads to hemoconcentration, prolonged bed rest studies have demonstrated that over a period of many days the hematocrit returns to normal values, presumably due primarily to suppression of red cell production (61, 75, 77). Bed rest for 4 weeks has reportedly produced a decrease of over 700 ml in blood volume (61, 75, 77). It should be pointed out, however, that in spite of the great amount of empirical evidence to the contrary, three well conducted bed rest studies of 14, 30 and 42 days in duration have yielded data indicating that after a typical initial decrease, blood volumes tended to return toward pre-exposure values (28, 67, 118).

Post-flight data on the command pilots and pilots of the 4 and 8 day Gemini missions indicated that the blood volume also decreases in the weightless environment (12). A 7 to 15 percent decrease of blood volume occurred during these missions. The decrease in plasma volume was 4 to 13 percent. As compared to bed rest studies, the loss of red cell mass was accelerated, possibly due to one or more factors other than blood volume changes, including the atmosphere to which the astronauts were exposed (12). It was also thought that a weight loss of usually 2 to 5 percent of body weight, recorded after these and all former space missions, might in part be due to this decrease of blood volume, especially since

weight loss did not correlate with mission duration, and pre-flight weights and plasma volumes were restored rapidly by fluid intake in the post-flight period<sup>(12, 124)</sup>. Immediately after the 14 day Gemini mission, however, the blood volumes of both astronauts were the same as those recorded pre-flight<sup>(12)</sup>. An increase of plasma volume had compensated for a decrease of red cell mass similar to that observed after the 4 and 8 day Gemini missions. It is clear that the results of the 14 day mission do not rule out the possibility that blood volume decreased during the early part of this mission. Interestingly, this data is supported by the few bed rest studies cited above.

A number of investigators have advanced reasonable explanations for the decrease of blood volume and the diuresis which occur during bed rest, complete water immersion and presumably on becoming weightless<sup>(5, 34, 35, 36, 51, 68, 70, 71, 110, 116, 124)</sup>. Negation of the gravitational component of intravascular hydrostatic pressures due to gravity leads to a redistribution of blood<sup>(90)</sup>. Sjöstrand<sup>(89)</sup> substantiated the earlier observations of Thompson<sup>(104)</sup>, by finding that about 500 ml of the approximately 650 ml of blood pooled in the lower extremities of erect man shifted on tilt to the thorax. As well, total blood volume actually increases slightly for a short period of time when a normal ambulatory individual assumes the supine position<sup>(9, 17, 58, 64, 104, 105, 127)</sup>. This is presumably due to the reabsorption of fluid transudate, forced by gravity-activated intravascular hydrostatic pressures into the extravascular spaces of loosely bound tissues in the lower extremities and elsewhere. Gauer and co-workers<sup>(5, 6, 33, 34, 36, 37, 38, 53, 58)</sup> have shown that due to this redistribution of blood, central venous channels are distended. This leads to stimulation of central venous blood volume receptors, located mainly in the right atrium. Through reflex pathways, antidiuretic hormone production is inhibited. The resulting increase in plasma water excretion reestablishes normal central venous volume. Other responses to this shift in blood volume also occur, although to a much lesser degree. Due to one or more possible mechanisms involving venous and possibly arterial volume sensors, and probably osmoreceptors, aldosterone production is suppressed, leading to a natruresis<sup>(31, 32, 44, 45, 54, 70, 94, 102, 103)</sup>.

Since this response is sluggish and highly variable, it appears that in this case the constancy of osmotic composition is sacrificed in favor of the constancy of blood volume (33, 54, 70, 80). Indirect evidence of a diuretic factor appearing in the blood plasma remains to be identified (34). Renal hemodynamics do not seem to be altered to a significant degree (20, 36, 70). Finally, experiments on normal individuals have shown that compensatory events opposite to those described above occur when central venous volume is lowered as a consequence of, for example, blood redistribution due to the force of gravity and measures which force or remove blood from the thorax, such as positive pressure breathing and the application of negative pressure to the lower half of the body (42, 44).

The question arises as to how much one or more factors other than simulated and actual weightlessness could have affected blood volume during bed rest and complete water immersion studies, and during the few space missions in which this parameter has been studied. For example, results from chair rest and confinement studies have shown that even though intravascular hydrostatic pressures due to gravity remained unaltered during these studies, subsequent physical inactivity is accompanied by a decrease in red cell mass and plasma volume (15, 62, 63, 65, 90). Since plasma volume decreases mostly during the first 48 hours of bed rest, and then changes little over a period of several weeks, it has been considered possible that physical inactivity might not enhance significantly the plasma volume contraction due to weightlessness per se (60). This possibility is supported by results of a few bed rest studies during which periodic exercise was performed (78, 112, 115, 117, 121). On the other hand, the decrease of red cell mass and further contraction of blood volume in most of the prolonged bed rest studies cited above might have been due in part to physical inactivity, for one might expect that blood volume would have been maintained by an increase in plasma volume, since homeostatic mechanisms restored the hematocrit to a normal level (124). This area does appear to require investigation.

A decrease in blood volume also accompanies body dehydration, which can be due either to inadequate fluid intake or to excessive loss of body water (60). The sensation of thirst can be markedly suppressed in

a stressful situation <sup>(52)</sup>. It is also well known that non-thermogenic sweating is increased in such a situation <sup>(124)</sup>. One wonders, therefore, if these factors existed to a significant degree during the critical terminal phases of space missions, and so accounted in part for the dehydration observed after all space flights to date and the decrease of blood volume recorded after the 4 and 8 day Gemini flights <sup>(12)</sup>. Sweating from heat loads experienced during re-entry and after landing might also have led to some dehydration <sup>(61)</sup>. Both physical and emotional stresses can suppress antidiuretic hormone production <sup>(61, 110)</sup>. Hence these too might have been factors producing dehydration, especially toward the end of space missions.

In conclusion, it is readily apparent that dynamic changes in the volume of blood, and in its plasma and red cell fractions while in the weightless environment, cannot be predicted with certainty at the present time. Definite answers in this area might only be obtained by further measurements on astronauts during space missions, with attempts to eliminate all factors other than weightlessness known to alter these parameters. Considerable evidence supports the view that blood redistribution in the weightless environment will lead to a decrease in blood volume, due initially to a decrease in plasma volume, and then to adjustments in both plasma volume and red cell mass as a normal hematocrit is gradually reestablished. On the other hand, there is evidence indicating that the blood volume could be diminished temporarily, possibly for only several days to a few weeks in duration. This rebound of blood volume, if it actually occurs, might be attributable to expansion of the venous circulation as peripheral venous tone, so important for preventing blood pooling in the gravity environment, relaxes as an adaptive response to weightlessness. On the other hand, the rebound of volume might be due to decreased sensitivity of blood volume receptors during chronic exposure to relatively high central venous pressure. This mechanism receives much off-on stimulation as a normal ambulatory individual moves about in the gravity environment, and like other reflex

mechanisms, may respond to chronic "on" stimulation by adaptation (86).

Other cardiovascular adaptations to weightlessness have been implied from observations made during passive upright tilt of bed rest and complete water immersion subjects, and post-flight astronauts. This is a provocative test of orthostatic tolerance. Since the individual is passively supported upright, it assesses the capacity of primarily cardiovascular mechanisms to compensate for intravascular hydrostatic pressure changes due to the force of gravity<sup>(113)</sup>. A minor reduction of orthostatic tolerance is accompanied by an excessive increase in heart rate, an excessive narrowing of pulse pressure and a fall in systemic arterial blood pressure while passively maintaining the erect posture<sup>(93)</sup>. Failure of cardiovascular compensation to gravity leads to the so-called vasodepressor reaction, the manifestations of which are presumably due to an overwhelming increase in parasympathetic nervous system activity<sup>(2, 59, 71, 92)</sup>. This reaction is characterized clinically by pallor, nausea, dimming of vision, sweating, "air-hunger" and eventually loss of consciousness, arising from an acute fall in systemic arterial blood pressure, occasioned by bradycardia and a decrease in peripheral vascular resistance<sup>(7, 30, 59)</sup>.

Definite signs and symptoms of orthostatic intolerance have consistently appeared after as little as one week of bed rest and 6 to 12 hours of complete water immersion<sup>(14, 28, 46, 47, 48, 49, 51, 77, 101)</sup>. Orthostatic intolerance was observed after the 9 and 34 hour, one-man Mercury missions<sup>(12)</sup>. Abnormal tilt responses were also noted for periods of up to 50 hours after the 4, 8 and 14 day, two-man Gemini missions<sup>(12)</sup>. The 14 day Gemini pilot experienced a vasodepressor reaction during his first post-flight tilt; his responses to subsequent tilts were similar to those of the other Mercury and Gemini astronauts. Interestingly, the time for the return of the normal pre-flight response to tilt has not correlated with either the duration of space flights to date, or decreases in blood volume which occurred.

As discussed by Lamb<sup>(59, 60)</sup>, McCally and Graveline<sup>(71)</sup>, and Vogt<sup>(106)</sup> and summarized below, many complex physiologic events are thought to

maintain cardiovascular integrity in the upright position. Hence it has been difficult to determine with certainty what cardiovascular adaptations to simulated and actual weightlessness might have occurred to account for the decreased orthostatic tolerance that resulted from exposure to these conditions. According to the above named authors, cardiovascular reflex mechanisms increase heart rate on becoming upright, and augment adrenal epinephrine output to strengthen cardiac muscle contraction. Arteriolar tone is also increased in dependent parts of the body to maintain the required distribution of cardiac output to these parts. Venous pooling in the lower regions of the body is minimized to assure an adequate return of blood to the heart. This appears to be accomplished mainly by a reflex increase in venous tone, by the restricting effect of skeletal muscle tone on venous distension, by the pumping action of contracting leg muscles on the veins and by venous valve competence. Through mechanisms outlined above, blood volume must also be maintained in the face not only of gravitational pooling of blood, but also of transudation of protein-free fluid into the extravascular spaces of the lower extremities caused by excess intravascular over extravascular pressures, especially in loosely bound tissues (104, 116). The tension created in tissues as fluid is forced into them would also serve to restrict venous distension.

There is no doubt that the decrease of blood volume and reabsorption of fluid transudate from tissues of the lower extremities during exposure to weightlessness would diminish orthostatic tolerance, since decrease of blood volume in a normal active individual from any cause, such as blood loss or dehydration, will result in a strain being placed on normal mechanisms required to maintain cardiovascular integrity in the upright position (3, 19, 52, 84, 99, 124). The observations that there has been no correlation between the amount of blood volume decrease and the degree of orthostatic intolerance resulting from prolonged bed rest, and that post-flight Gemini astronauts demonstrated orthostatic intolerance for many hours after their blood volumes returned to pre-flight levels, suggest that cardiovascular adaptations to weightlessness other than decrease in blood volume contributed to this orthostatic intolerance (78, 94, 100, 126).

Since skeletal muscle loses tone, strength, work capacity, and mass when its activity is diminished for a period of time, the question arises as to whether smooth muscle in a blood vessel wall could undergo similar changes when it no longer plays a role in maintaining the wall tension required to compensate for the gravitational component of intravascular hydrostatic pressure. If so, this adaptive response would be expected to occur both in arterial vessels, especially arterioles, and in veins in dependent parts of the body, and thus predispose to orthostatic intolerance by failing to maintain normal distribution of cardiac output and by allowing excessive pooling of venous blood. This might well be a fruitful area for study.

It has been postulated that the mechanisms responsible for increasing arteriolar resistance and venous tone in the upright position become less responsive during prolonged exposure to weightlessness (42, 68, 71, 105, 109). Reflex vasoconstriction, as occurs on assuming an upright posture, is known to be mediated by the sympathetic nervous system, the vascular nerve endings of which release norepinephrine to cause vascular smooth muscle contraction (13, 28, 74, 122, 123). As shown by tilting normal active individuals to various angles, changes in the urinary excretion of norepinephrine correlate well with alterations in vasomotor activity (98). Hence various investigators have suggested that diminished responsiveness of vasoconstrictor mechanisms by weightlessness might be reflected by decrease of urinary norepinephrine excretion during upright tilt (43, 47, 105). Such was the case following complete immersion of subjects for 6 hours in one study, but not the case in the other similar study in this area (43, 105). Further investigation is therefore required to determine at what neuromuscular level vasoconstrictor mechanisms adapt to weightlessness.

A few other cardiovascular adaptations to weightlessness per se have been implicated as contributors to the decreased orthostatic tolerance after simulated and actual weightless exposures. Since the sympathetic nervous system is also presumed responsible for the cardioacceleration and the increase of adrenal epinephrine output associated with assuming upright posture, it has been suggested that these responses might be

diminished by weightlessness<sup>(106)</sup>. However, no evidence has been obtained in this area. Since tension exerted on veins by extravascular tissue is thought to play an important role in preventing venous pooling in the upright position, loss of fluid transudate from tissues of the lower extremities in the weightless environment might enhance venous pooling as well as loss of blood volume in the erect position, hence contributing, especially in the very immediate period after re-exposure to gravity, to orthostatic intolerance.

An enhanced tendency to venous pooling on assuming an upright posture does appear to be a major effect of simulated and actual weightlessness. Increases of venous engorgement and leg circumference, and dependent cyanosis have been observed during tilt of individuals subjected to prolonged periods of bed rest<sup>(28, 46, 78)</sup>. In fact, blood congestion has reportedly been great enough to produce purpuric hemorrhages about the feet and ankles, even though blood platelet and prothrombin levels were normal<sup>(28)</sup>. It has also been thought that strain gage data obtained on post-flight Gemini astronauts confirmed pooling of blood in their lower extremities for the period of time required for their tilt responses to return to normal<sup>(12)</sup>. The adaptive changes, and the relative contributions of such changes responsible for venous pooling remain to be determined.

With respect to the possible contribution of physical inactivity, the foregoing discussion indicated that failure to maintain skeletal muscle strength, tone, and mass would reduce the restrictive effect which extravascular tissue tension exerts on venous distension and possibly somewhat diminish the pumping effectiveness of muscle contraction, or even be severe enough that this effect, in combination with inadequate venous tone and diminished tissue turgor, could lead to venous valve incompetence. It is also wondered if physical inactivity could diminish the capacity of arterioles and veins to maintain adequate tone, or the responsiveness of vasoconstrictor and cardiac stimulating mechanisms required to maintain cardiovascular integrity on assuming an upright position. Miller<sup>(78)</sup> found that the dependent cyanosis associated with prolonged bed rest could be reduced with exercise. Hence it was suggested



that inactivity could have an effect on venous pooling, possibly through an associated loss of arteriolar or venous, or skeletal muscle tone. However, as will be discussed subsequently, attempts to reduce orthostatic intolerance from prolonged exposure to simulated and actual weightlessness by periodic exercise during exposure have on the whole proven unsuccessful. Moreover, one would not expect physical inactivity to contribute to orthostatic intolerance observed after 6 to 12 hours of complete water immersion, especially since the immersed subjects were usually unrestricted in movement. Thus it would appear that cardiovascular adaptations to weightlessness have overshadowed the role played by physical inactivity in producing the orthostatic intolerance observed after prolonged bed rest, complete water immersion and weightless exposures to date. More conclusive information in this area is still required.

A few other factors have been considered possible contributors to the post-flight orthostatic intolerance observed in astronauts. It must be kept in mind that their significance is difficult to judge, especially since they were not present in simulated weightlessness studies. It is a well established fact that post-flight fatigue, which has been observed to some degree in all post-flight astronauts to date, tends to increase the susceptibility to orthostatic intolerance<sup>(59)</sup>. The possible occurrence of mild dehydration which, through an associated decrease in blood volume, could be a factor in producing orthostatic intolerance in the immediate post-flight period has been discussed above. Finally, it has been considered possible that orthostatic intolerance might be contributed to by physiologic events which might be associated with the vague feeling of "let-down" often experienced after a prolonged emotionally and physically stressful event, such as a space mission<sup>(59)</sup>.

In conclusion, studies of tilt responses of individuals who have been exposed for prolonged periods of time to simulated and actual weightlessness have indicated that the adaptive response of the cardiovascular system is not restricted just to blood volume changes. Although a decrease in blood volume no doubt contributes causally to orthostatic intolerance observed after such exposures, there is both direct and indirect evidence that the

ability of the cardiovascular system to maintain its integrity in the upright position decreases during exposure to the weightless environment. This is generally thought to result primarily from an enhanced tendency to venous pooling, the etiology of which remains to be determined. It has been postulated that arteriolar and cardiac responses to the upright position might also be involved.

### Medical Implications

Other chapters in this report point out the fact that many of the medical problems which might arise from hazards of space operations can be influenced by, and have profound effects on the functional integrity of the cardiovascular system. In the light of the foregoing discussion in this chapter, one wonders what effects cardiovascular adaptations to weightlessness might have on medical problems. This very important area of clinical space medicine has received little attention to date. Hopefully, the following considerations will stimulate further thought and investigation in this area.

As the result of a decrease of blood volume associated with weightlessness, an astronaut who suffers "shock" in space will, in essence, not receive the benefit of the "transfusion" of pooled blood which a normal ambulatory individual on Earth receives on assuming the supine position. As well, it will not be possible in space to enhance brain blood flow of an astronaut in "shock" by tilting him to the head-down position. If blood volume actually returns to its pre-mission level as exposure to weightlessness continues, one would expect that an astronaut's susceptibility to "shock", especially from decrease of blood volume, would be somewhat reduced.

Otherwise, there is no reason to believe that the mechanisms which compensate for threats to the functional integrity of the cardiovascular system, such as blood loss or myocardial damage, should be any less efficient in the weightless environment than on Earth. This assumes of course that cardiovascular "fitness" is maintained at an optimum level in space. The absence of hydrostatic forces due to gravity should, in fact,

allow an astronaut to tolerate cardiovascular stresses better while moving about in space than while moving about on Earth. Since hydrostatic forces due to gravity play a great role in producing the vasodepressor reaction, be it on the basis of pain, heat load, postural blood shift or pathophysiologic reflex, this reaction might be much less likely to occur or to progress on to the syncopal stage in space than on Earth.

The cardiovascular adaptations to weightlessness are of great concern to an astronaut who is re-exposed to a gravity environment during exploration of a lunar or planetary surface, or is subjected to accelerative forces in the head-to-foot direction during take-off and landing operations. It is noted that data obtained during passive upright tilt of individuals who have been exposed for prolonged periods of time to simulated and actual weightlessness do not allow prediction of risks of the vasodepressor reaction facing astronauts while standing or moving about in gravity environments. This provocative test of cardiovascular function allows neither the pumping of venous blood by contraction of muscles of the lower extremities, nor the restriction of venous distension by the tone of these muscles associated with weightbearing. Accordingly, it is thought that if physical, and in turn cardiovascular "fitness" is maintained, the risks of an astronaut experiencing a vasodepressor reaction from orthostatic intolerance due to the effects of only the cardiovascular adaptations to weightlessness will probably be quite low, especially during operations in environments with gravitational forces less than that on Earth. This view is supported by the fact that astronauts have apparently not experienced manifestations of orthostatic tolerance while standing and walking about in the post-flight period. It should be noted, however, that the decrease of circulating blood volume associated with orthostatic intolerance will reduce physical work capacity, whether or not orthostatic intolerance is clinically manifest <sup>(124)</sup>. Thus there is obviously a great necessity for studies oriented toward determining not only the effects which cardiovascular adaptations to weightlessness can have on astronauts during operations in various gravity environments, but also the need for measures which confer protection from these effects.

As would be expected, prolonged exposure to simulated weightlessness has been found to markedly reduce tolerance to accelerative forces applied in the head-to-foot direction (10, 11, 99). If cardiovascular fitness is maintained in space, there is no reason to believe that cardiovascular adaptations to weightlessness will alter an astronaut's tolerance to transversely applied accelerative forces associated with landing and take-off operations (75).

It is readily apparent from foregoing discussion that cardiovascular adaptations to weightlessness will render the cardiovascular system less able to maintain its functional integrity in the upright position when it is challenged by various stresses (3, 38, 43, 65, 66, 80). One stress is a further reduction of blood volume by such factors as hemorrhage, plasma loss and dehydration. Another stress is an expansion of circulatory capacity, as occurs on exposure to heat, with exercise or during a vasodepressor reaction. Then too, inadequate cardiac output could result from an imposed stress of impeded return of blood to the heart by, for example, a constricting garment or pressure breathing.

Circulatory adjustments required to maintain orthostatic tolerance in the face of cardiovascular adaptations to prolonged weightlessness might conceivably increase the risk of an astronaut developing a medical problem during operations in a gravity environment. For example, the decrease in peripheral blood flow associated with orthostasis might be sufficient to render an astronaut more susceptible to cold injury or a heat disorder.

Finally, since any degree of orthostatic intolerance is associated with diminished cerebral perfusion and hence borderline cerebral hypoxia, it is thought that cardiovascular adaptations to weightlessness might reduce significantly an astronaut's "time of useful consciousness" on exposure to a low partial pressure of oxygen after return to a gravity environment (Chapter 1), even though lung-to-brain circulation time would be lowered. This hypothesis does require experimental verification.

## Protective Measures

Foregoing discussion has pointed out the need to assure an astronaut that he will not suffer from the adverse effects of cardiovascular adaptations to weightlessness on being re-exposed to a gravity environment during exploration of a lunar or planetary surface, or on being subjected to head-to-foot accelerative forces during take-off and landing operations. There are two general preventive approaches, the investigative status of which has been periodically reviewed (60, 71, 75, 85, 117, 126).

The one approach is to prevent the occurrence of cardiovascular adaptations to weightlessness. The other is to protect the astronaut from the adverse effects of these adaptations. Those methods which have received consideration and study to date in attempts to accomplish these approaches are outlined below. Particulars of their application can be obtained from cited references. Although some indication of their effectiveness can be given, it must be remembered that appropriate selection and optimum utilization of a particular method will be assured only by more intensive investigation in this area.

The greatest attention from the standpoint of preventing cardiovascular adaptations to weightlessness has been focused on periodic physical exercise as a way of maintaining an optimum level of physical "fitness" during space missions. Since exercising increases blood volume in a normal ambulatory individual on Earth, it was thought that an appropriate exercise regimen might minimize the decrease of blood volume associated with weightlessness (16, 21, 22, 27, 77, 90). As well, exercising the lower extremities in particular might reduce the tendency to venous pooling by maintaining muscle tone, strength and mass, and possibly to some extent the capacity of vasoconstrictor mechanisms to respond to intravascular hydrostatic forces due to gravity (60). However, a number of isotonic and isometric exercise regimens have reportedly had no really significant effect on either the blood volume or the degree of orthostatic intolerance associated with prolonged bed rest (16, 25, 27, 76, 109, 112, 117, 121, 125, 126). Bungee cord exercises during the 8 and 14 day, two-man Gemini missions were also not protective, even though the cardiovascular

response to a calibrated work load might for the most part have been maintained by these exercises (12, 91). If exercise will ever be a method which could be used in space specifically for the prevention of cardiovascular adaptations to weightlessness is doubtful, but further study in this area still appears indicated.

Various combinations of periodically inflated cuffs placed proximally on the extremities have been used in attempts to prevent cardiovascular adaptations to weightlessness. It was thought that periodic increases of intravenous hydrostatic pressures, especially in the extremities, might maintain not only venomotor capacity but an optimum level of extravascular tissue tension during prolonged space missions (26, 29, 71). Another effect postulated was reduction of the degree of central venous volume overload, and hence decrease of blood volume associated with weightlessness (26). Indeed, Graveline (46) and then Vogt (111), found that periodic inflation of cuffs placed around all four extremities of subjects immersed up to the neck in water for 6 hours maintained orthostatic tolerance. When carried out during two weeks of bed rest, this technique conferred significant protection from orthostatic intolerance as tested by a 10 degree tilt, which presumably simulated the effect of the Moon's gravitational field on the cardiovascular system (76). On the other hand, a variety of cuff configurations applied during a number of water immersion and prolonged bed rest studies have been unsuccessful in preventing either decrease of plasma volume or orthostatic intolerance (25, 73, 96, 112, 114, 117). Periodic inflation of lower extremity cuffs on the pilots of the 8 and 14 day two-man Gemini missions was also ineffective in lessening post-flight orthostatic intolerance, even though there appeared to be some decrease in the degree of post-flight pooling of blood in the lower extremities as judged by the strain gage technique (29, 91). Thus it has been concluded that in the light of failure to establish definite effectiveness of extremity cuffs in many simulated and actual weightless exposures to date, further consideration of the use of cuffs in the space flight situation is not warranted (114).

Exposure to lower-body negative pressure has been suggested as a method of preventing adverse effects of cardiovascular adaptations to

weightlessness, since its effect on the cardiovascular system is similar to that of increasing the gravitational component of hydrostatic pressure (60, 93). It was thought that forced pooling of blood in the lower part of the body would serve to stimulate expansion of circulating blood volume by mechanisms outlined above (60). Another effect anticipated was transudation of fluid, due to increased intravascular pressures, to rehydrate and restore tension to tissues of the lower extremities, possibly to pre-mission levels (60). Although lower-body negative pressure has been found to produce less of an increase in peripheral venous tone than standing, this technique might conceivably restore to some degree the capability of veins and, if they are also affected by weightlessness, arterioles to respond to intravascular hydrostatic pressures due to gravity (4, 40). A number of studies have shown that lower-body negative pressure can either prevent or restore the decreases of plasma volume and orthostatic tolerance which result from prolonged bed rest (16, 40, 64, 72, 78, 95, 97). Of particular importance in terms of space missions of long duration is the fact that orthostatic tolerance was restored with this method over a period of only 2 days (60, 95, 97). Hence for space missions of any length of time, orthostatic tolerance could be reestablished on a short-term basis just prior to entering a gravity environment (60). Although exposure to lower-body negative pressure appears to be a very feasible measure for restoring an astronaut's orthostatic tolerance while in space, possible restrictions which this measure might place on an astronaut's activity during a critical phase of a mission must be taken into account. There is also an apparent need for studies aimed at determining time and pressure modes which would provide an optimum effect.

Again, in an attempt to readapt the cardiovascular system to gravity, periodic centrifugation has been assessed for its effectiveness in preventing orthostatic intolerance resulting from prolonged bed rest. White (125, 126) has reported that as little as four 7.5 min rides on a short-arm centrifuge largely prevents orthostatic intolerance as judged by syncope. However, heart rate and blood pressure responses to tilt, and decrease of plasma volume during bed rest, were essentially unaffected by this

measure. Interestingly, the steep heart-to-foot acceleration gradient of 256 percent created by this measure did not preclude movement of the head, arms and legs, and motion sickness was not a problem for the well trained individual when exposed to high angular rates and modest head or limb movements. Further testing of periodic centrifugation appears indicated <sup>(126)</sup>. It is considered possible that the weight, power and volume penalties imposed by a short-radius centrifuge could be brought into perspective for spacecraft of the future, if the effectiveness of this measure is well established.

A few other protective measures which have been suggested for use in space have been studied, all being essentially ineffective in experiments to date. The administration of 9-alpha, fluorohydrocortisone for a short period of time towards the end of prolonged bed rest exposures did return blood volume to normal and in fact often above normal, but did not prevent the orthostatic intolerance resulting from these exposures <sup>(57, 94, 96)</sup>. It should also be noted that this drug produced occasional nausea, an effect which would be highly undesirable in the space situation <sup>(96)</sup>.

Presumably to stimulate peripheral vasomotor reflexes otherwise dormant during exposure to weightlessness, variants of positive pressure breathing have been applied. However, they have had no significant effect on the orthostatic intolerance resulting from head-out water immersion and bed rest <sup>(55, 115)</sup>.

The administration of pitressin, with and without concomitant water-loading to subjects immersed to the neck in water has prevented the diuresis, and associated decrease in plasma volume, but not the orthostatic intolerance which results from water immersion <sup>(55, 56, 73)</sup>.

Based on the fact that many of the physiologic responses to hypoxia are the reverse of those to weightlessness, individuals have been exposed to 10,000 to 12,000 ft altitudes during bed rest <sup>(60, 61, 95, 97)</sup>. Although exposure to mild hypoxic conditions did prevent the decrease in red cell mass which occurred during bed rest exposures at ground level, it did not reduce the orthostatic intolerance produced by bed rest.

Periodic bouncing exercise on a railed cart between two trampolines has been carried out on prolonged bed rest subjects <sup>(27)</sup>. It was thought



that the vascular stimulation of exercise, as well as the repetitive "sloshing" of blood, would serve to maintain the capacity of both veins and arteries to compensate adequately for intravascular hydrostatic forces due to gravity. Although this measure was found ineffective, it might warrant further testing.

What appears to be the most effective measure assessed to date for the protection of bed rest and water immersion subjects from orthostatic intolerance has been the application of a pressure garment to the lower part of the body during tilt. The external pressure primarily acts to prevent excessive venous pooling and excessive loss of plasma volume through transudation of fluid into the tissues of the lower extremities in the upright position <sup>(60)</sup>. The partial pressure, or so-called "anti-G" suit has been used to prevent fainting of individuals suffering from postural hypotension <sup>(82)</sup>. Orthostatic tolerance after 6 hours of head-out water immersion was improved, beyond the pre-immersion tolerance with an elastic gradient leotard <sup>(73)</sup>. The partial pressure suit has been proven effective in preventing orthostatic intolerance after prolonged bed rest <sup>(76, 77)</sup>. It is therefore believed possible that any effective pressure garment that can be applied by an astronaut prior to re-exposure to a gravity environment will provide a large measure of protection against a possible significant decrease in orthostatic intolerance <sup>(60)</sup>. The most suitable garment would appear to be the Jobst stocking or elastic leotard. They can be adequately ventilated and permit normal body movement, and can be easily donned. In such a garment, one could perform normal activities.

Finally, protection from adverse effects from cardiovascular adaptations to weightlessness might be a factor coming into considerations of whether to provide astronauts artificial gravity in space. It is readily apparent from above discussion that the weight this factor should have in reaching this decision remains to be established. If artificial gravity is employed, the level required for preventing orthostatic intolerance in various gravity environments to be encountered during space missions will have to be determined.

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## CHAPTER 11

### ACUTE RADIATION EFFECTS

Assessments of the presently known and anticipated radiation hazards in space are indicating that serious acute radiation effects should not be suffered by astronauts if adequate precautions are taken. One must remember, however, that current information on ionizing radiations, particularly from solar flares in space, is based on relatively sparse data. Therefore, it is still considered necessary to assume that there could be a requirement for the treatment of acute radiation effects in space. This chapter briefly outlines the acute medical problems which result from unexpected exposure of astronauts to various radiations during space missions. Emphasis is placed on the characteristics and management of ionizing radiation effects which are presently thought most likely to occur following exposure to solar flare radiation.

Various radiation terms to be used in this chapter are defined in Figure 11.1. The relative biological effectiveness (RBE) of a particular type of radiation is a multiplier which equates the biologic response of this radiation to that of X or gamma radiation having a linear energy transfer (LET) equivalent to 3 Kv/ $\mu$  of water and being delivered at the rate of 10 rads/min. When an RBE value is used for a specific biologic endpoint, it is commonly referred to as a quality factor (QF).

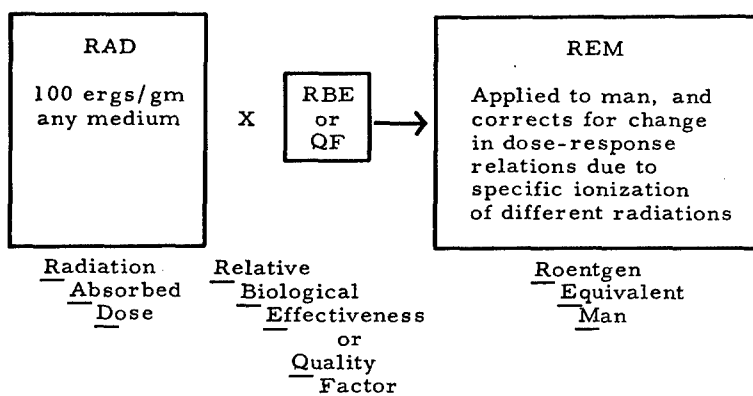


Figure 11.1 Radiation Terms

## Space Radiation Hazards

The various radiations to be expected in the space environment have been discussed extensively in the literature. Therefore they are dealt with briefly below, with major references from which further detail can be obtained being cited.

### Trapped (Van Allen) Radiation

Because flight plans usually call for orbits beneath or transient passage through the zones of geomagnetically trapped radiation surrounding the Earth, this source is considered a relatively minor hazard to astronauts. The location and characteristics of the zones are being so precisely defined that depending on the spacecraft shielding and trajectories selected, radiation exposure can be maintained at safe levels during both orbiting and non-orbiting missions. It is conceivable, however, that during an emergency extravehicular operation on the fringe of a zone, or intra-vehicular operations within the zones, there might be a danger of skin injury from high energy particles <sup>(117)</sup>. Radiation zones around planets being explored are yet to be identified and their characteristics thoroughly studied.

### Artificial Radiation Belts

Artificial radiation zones of high energy electrons can be created by nuclear explosions in space. They could present a serious biologic hazard, especially to orbiting astronauts. The dose of radiation an astronaut could receive will depend on pre-flight planning and the amount of contingency exposure in flight. Dose rates measured four months after the Starfish nuclear explosion in space were dangerously high, at 30 rads/hr behind  $4.5 \text{ gm/cm}^2$  brass shielding <sup>(18)</sup>. Due to flux decay, the dose rates were below 0.2 rad/day behind  $5 \text{ gm/cm}^2$  aluminum two months later. Such a dosage would not produce acute radiation effects.

### Galactic Cosmic Radiation

Galactic cosmic radiation is believed to originate outside of our solar system, but within our galaxy <sup>(28)</sup>. This radiation consists of extremely

high energy atomic nuclei, of which approximately 86 percent are protons, 13 percent are alpha particles and the remainder are elements of higher atomic number <sup>(120)</sup>. Since cosmic particles produce discreet dense ionization tracks in tissues, the possibility that they might seriously injure such vital organs as the lens of the eye, the retina, the hypothalamus, or the brain has been considered. Schaefer <sup>(97)</sup> has recently estimated that exposure to galactic cosmic radiation in free space would have a significant life-shortening effect, possibly as much as 20 percent. Inadequate simulation in ground-based experimentation and biologic exposures in space have precluded definitive evaluation of this hazard <sup>(25, 26, 94)</sup>. Otherwise, unless streams of cosmic radiation exist in space, these particles are so few in number that they do not now appear to be an acute hazard to astronauts <sup>(65, 94)</sup>. The average whole-body dose rate of this radiation in free space is generally thought to be about 5 rads/yr during the period of maximum solar activity and about 15 rads/yr during minimum solar activity <sup>(1, 41, 42, 47, 73, 80, 97)</sup>. It is noted that the latter dose is just about 100 times larger than the background dose at sea level on the Earth <sup>(97)</sup>.

#### Radiation Sources On Spacecraft

Nuclear energy used for propulsion or as a source of power during space flight should not be a radiation hazard if adequate precautions are taken to ensure protection of astronauts both during normal operations and in an emergency. By the same token, it is assumed that astronauts will be adequately shielded from the strong magnetic fields which might be used in magnetohydrodynamic propulsion or for repelling high energy solar flare protons from the spacecraft hull, and from microwaves emanating from activated radar systems.

#### Solar Electromagnetic Radiation

Solar electromagnetic radiation should not be hazardous to an astronaut who is adequately shielded by the wall of his spacecraft or by his space suit. The radiant energy output of the sun in the ultraviolet, visible, and infrared spectrum is remarkably constant in spite of the

occurrence of sunspots and associated activity <sup>(94)</sup>. Even though adequate measures will presumably be taken to maintain environmental temperatures in space at comfortable safe levels, it is still considered possible that breakdown of a temperature control system could cause an astronaut to suffer from a heat disorder (Chapter 6).

The visual spectrum can be dangerous in that the warning glow seen on Earth as the line of sight approaches the sun is not seen in space. Filtration of sunlight must be adequate to prevent temporary retinal effects such as glare or flash-blindness or permanent retinal burns, both of which could result from inadvertent glances by unprotected eyes at the sun. These disturbances are discussed in detail under meteoroid "flash" in Chapter 12.

The types of plastics used for visors or windows offer adequate protection from ultraviolet light. In selecting materials for the space suit visor, it must be kept in mind that repeated protracted exposures to ultraviolet light during extravehicular operations necessitate an optimum degree of protection <sup>(45)</sup>. If not, this radiation, especially at wave lengths shorter than  $0.32\mu$ , could damage the surface cells of the eye, leading to the condition variously known as "snow blindness", and sunlamp or welder's keratoconjunctivitis. Associated signs and symptoms, which characteristically appear after a latent period of up to several hours, are severe eye pain, photophobia, conjunctival congestion and swelling, marked lacrimation, disturbances of vision, a granular appearance within the corneal epithelium, and with relatively severe exposures, cloudiness of the corneal stroma. Although the pain can be controlled with a topical anesthetic and cold compresses to the eyelids (Chapter 8), this condition usually heals in one to several days. An astronaut could be seriously incapacitated by this condition, especially if he is extravehicular at the time of its onset or requires full visual function to perform a critical task.

Solar x-rays, even from the solar flares to be discussed below, appear to be of too low energy and flux rate to penetrate a spacecraft or space suit and administer a significant harmful dose of radiation to an astronaut.



### Solar Particulate Radiation

Solar "Wind" - A large number of particles, mainly protons and electrons, are continuously given off by the sun (27, 47, 48).

Even during periods when the sun is more active, the kinetic energy of this plasma, or so-called solar "wind", does not reach levels which are high enough to cause concern as a radiation hazard to occupants inside of the spacecraft. On the other hand, this radiation must be carefully studied to determine whether or not it could be a potential hazard, especially to the skin, during extravehicular activity.

Solar Flares - Radiation emitted into space by the so-called solar flares or solar cosmic ray events presents the most uncertain and probably by far the greatest potential biologic radiation hazard in space. Therefore this hazard is discussed here in some detail, with emphasis being placed on anticipated flare characteristics which determine the risk of a serious exposure, the type and severity of acute radiation effects, and thus the possible requirements for the treatment in space of medical problems from radiation.

A solar flare is usually a short-lived increase in radiation intensity originating in the vicinity of a sunspot, persisting up to several days at any point in the solar system <sup>(94)</sup>. The higher energy components of the radiation flux from a flare is comprised mainly of protons with energies ranging from 10 Mev to a few Bev. Since these particles are the most biologically hazardous component, most shielding and biologic considerations have dealt only with them. Alpha particles can be nearly equal to or, on occasion, even greater in number than protons over a period of time during an event <sup>(47)</sup>. The contribution of alpha particles to the total biologic hazard is less well defined than is the case for proton radiation, although much is known of their biologic effects <sup>(52, 96)</sup>. Very little information is available on the distribution within flares and the biologic effects of heavier particles <sup>(87, 116)</sup>. The electromagnetic (e.g., ultraviolet, x-ray, gamma) components of a flare are not considered

a significant hazard to an astronaut behind typical space suit shielding (47, 53, 94).

The number of solar cosmic ray events follows the 11 year sunspot cycle in that these events tend to occur with greater frequency during the high incidence range of the cycle (80). As shown in Table 11.1, the past cycle, which has allowed the first accurate studies of flare and sunspot occurrences, began in 1954, reached a maximum early in 1958, and reached a minimum in 1965. From this cycle it appears that even though the greatest number of events take place at sunspot maximum, most of the major events might occur from one to 2 years after this maximum (47, 53, 73). Since over a period of many decades, the frequencies of sunspots and flares appear to correlate, long term (years) predictions of sunspot size, nature and frequencies might also be rough forecasts of future radiation hazards. On the other hand, there are at present apparently no substantial criteria for making short term (hours) predictions of solar flares (40, 94).

The arrival time and flux of solar flare protons at a point in space are related to the original velocities of the protons and the influence of magnetic fields in space. There is a delay from minutes to hours in the arrival of these particles, and their flux can be so dispersed that they can continue to arrive over a period of hours to days. Webber and Freier (122) have pointed out that for all flares, the protons with higher energies are detected sooner, and have a shorter rise time (time to reach maximum intensity) and a shorter decay time than protons with lower energies. Moreover, the flux decay of protons above a particular energy is exponential at most times for a wide range of proton energies (122). With these characteristics of a solar flare applied to measured flux-time profiles of protons above certain energies, it may be possible to reasonably predict the magnitude of a flare from measurements made by instruments which not only integrate dose but also differentiate energies during the early part of an arriving flare. This knowledge could then indicate whether or not special shielding measures or, if such is available to astronauts, a radio-protective drug is required to prevent radiation injury.

Event Date	Exposure (Rads)				
	Shielding gm/cm <sup>2</sup>				
	1.0	2.0	5.0		
2-23-56	309.0	185.0	103.0		
8- 3-56	9.1	5.3	2.4		
1-20-57	112.0	45.8	7.1		
8-29-57	78.7	26.2	3.5		
10-20-57	19.3	10.0	4.7		
3-23-58	1.5	0.6	0.1		
7- 7-58	156.0	55.0	9.6		
8-16-58	24.0	9.3	1.7		
8-22-58	46.0	15.3	2.0	48.0	6.9
8-26-58	81.2	23.4	3.2		
9-22-58	4.4	1.3	0.2		
5-10-59	484.0	217.0	66.8		
7-10-59	440.0	220.0	86.0		
7-14-59	675.0	312.0	91.0	728.0	253.8
7-16-59	392.0	196.0	76.8		
4- 1-60	2.0	1.0	0.5		
4-28-60	2.2	1.1	0.4		
5- 4-60	2.3	1.2	0.6	3.2	1.3
5-13-60	1.9	0.9	0.3		
9- 3-60	13.5	7.0	3.2		
9-26-60	1.2	0.5	0.1		
11-12-60	511.0	260.0	117.0		
11-15-60	295.0	142.0	64.9	410.9	185.7
11-20-60	17.9	8.9	3.8		
7-11-61	1.5	0.7	0.2		
7-12-61	26.3	8.8	1.2		
7-18-61	132.0	63.0	25.2	72.5	27.0
7-20-61	2.0	1.0	0.4		
9-28-61	2.4	1.1	0.5		
10-23-62	0.1	0.0	0.0		

Table 11.1 Integral Unit Sphere Free-Space Proton Exposures Under 1, 2, and 5 gm/cm<sup>2</sup> Aluminum Shielding for Major Cosmic Ray Events Occurring During Solar Cycle 19.

(After Langham, Brooks and Grahn (65)).

Because the proton flux from a solar flare event is widely distributed in energy and direction, and varies among different events and at different times during an event, no average biologic hazard can be described for solar flares. As shown in Table 11.1, the biologic hazard can be markedly modified due to a number of solar flares occurring over a period of several days. Finally, it should be kept in mind that until the next predicted period of maximum solar activity in 1969, few direct measurements of flares will have actually been made in free space.

Since shielding on most dosimeters has not allowed an adequate assess-

ment of the low energy radiation spectrum in space, the possible hazard of low energy protons and alpha particles to astronauts during extravehicular activity in free space remains to be defined. Solar flares which occur frequently and emit low energy protons are being identified (48). These and the solar "wind" might be a skin hazard and require investigation for evaluation of shielding provided by space suit materials.

The air dose rate of radiation imposed on an astronaut in a spacecraft being bombarded by solar flare protons will be determined primarily by the energy-flux characteristics of the protons stream, the type (atomic weight), thickness and geometry of the spacecraft shielding and by the astronaut's spatial position in the spacecraft. Figure 11.2 illustrates the effect of shielding thickness on air dose rate from incident protons. It is noted that neutrons contribute negligibly to the total dosage at shielding thicknesses of less than  $10 \text{ gm/cm}^2$  aluminum (72, 123). Short electromagnetic waves produced by the interaction of protons with such a metal of low atomic weight can also be considered insignificant (65, 72, 94, 123).

Integral cabin air doses as a function of spherical shielding thickness have been estimated for a number of flares of the last solar cycle (Table 11.1). Since a better understanding of the contribution of high energy particles to the total flare dose was brought into these calculations, the data are considered the most accurate available up to the present time. Table 11.1 lists only solar flare events for which there was sufficient flux data to justify free-space dose estimates. The effect of shielding in attenuating solar flare radiation dosage is again well demonstrated. Assuming that such data are reasonably correct, it will become evident in subsequent discussions that only the cumulative doses from two solar flare series (1959 and 1960) would have been sufficient to have had a significant effect on an astronaut in a spacecraft providing him spherical shielding of from 2 to  $5 \text{ gm/cm}^2$  aluminum.

Results of model calculations of proton depth-dose patterns using data of various flares are shown in Figures 11.3 and 11.4. Both serve to illustrate the marked decrease in tissue dose with increasing depth from

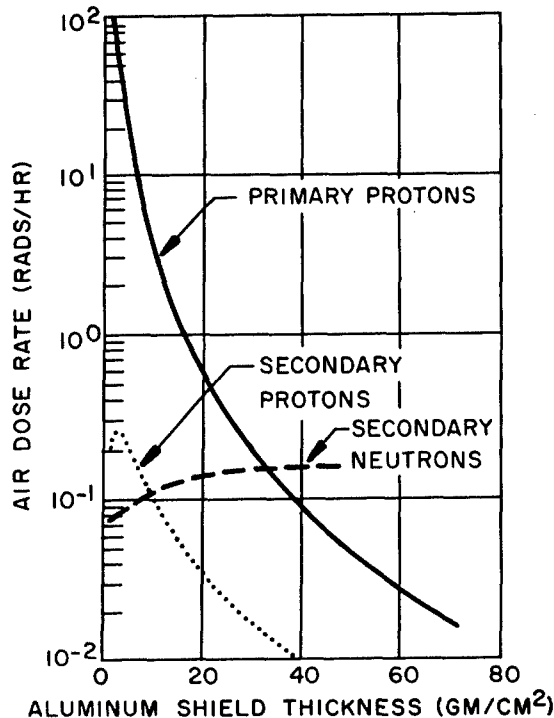


Figure 11.2 Calculated variations of primary and secondary point-target air dose rates as a function of the thickness of a spherical aluminum shield for the May 10, 1959 solar flare spectrum, measured 33 hours after onset.

(After Langham *et al*, <sup>(65)</sup> redrawn from Wilson and Miller <sup>(123)</sup>).  
the skin surface. Figure 11.3 represents calculated depth-dose patterns for three different solar flare rigidities considered representative of past flares. It is noted that even for the most energetic incident flare spectrum the tissue dose drops from about 30 percent of the skin surface dose at 5 cm depth. Figure 11.4 shows the depths of critical organs and tissues in relation to depth-dose distribution, in a spherical phantom, calculated for the May 10, 1959 solar flare event.

If past solar flare flux-energy-time, shielding, and tissue depth-dose data presented above are valid for predicting future radiation hazards in free space from flares, one can say with reasonable confidence that the occurrence of serious injury to deep tissues, such as the hematopoietic system and gastrointestinal tract, from a flare or series of flares with the order of magnitude and separation of those recorded in the last solar

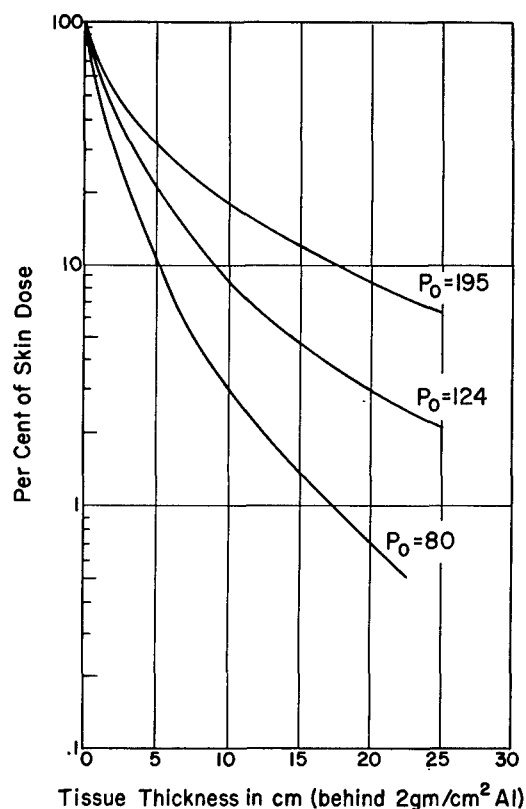


Figure 11.3 Tissue dose variation with increasing depth from skin for various incident flare spectra ( $P_0$  represents the rigidity, or spectrum of particle momenta at the time of maximum flare intensity).

(After Jones et al (61)).

cycle, will be highly unlikely. The skin may, however, be damaged under these conditions.

The acute skin dose of 200 KVP x-rays required to produce erythema is about 650 to 700 rads (65). As shown in Figure 11.5, protraction of exposure allows some repair of skin damage to take place during exposure, so that the dose required to produce erythema is increased. By the same token, Figure 11.6 demonstrates that previous skin exposure reduces the allowable next dose because of residual unrepaired damage. If it is assumed that solar flare protons and 200 KVP x-rays have the same QF for skin injury, and solar flare data in Table 11.1 are reasonably accurate, then Figures 11.5 and 11.6 indicate that past flares and series

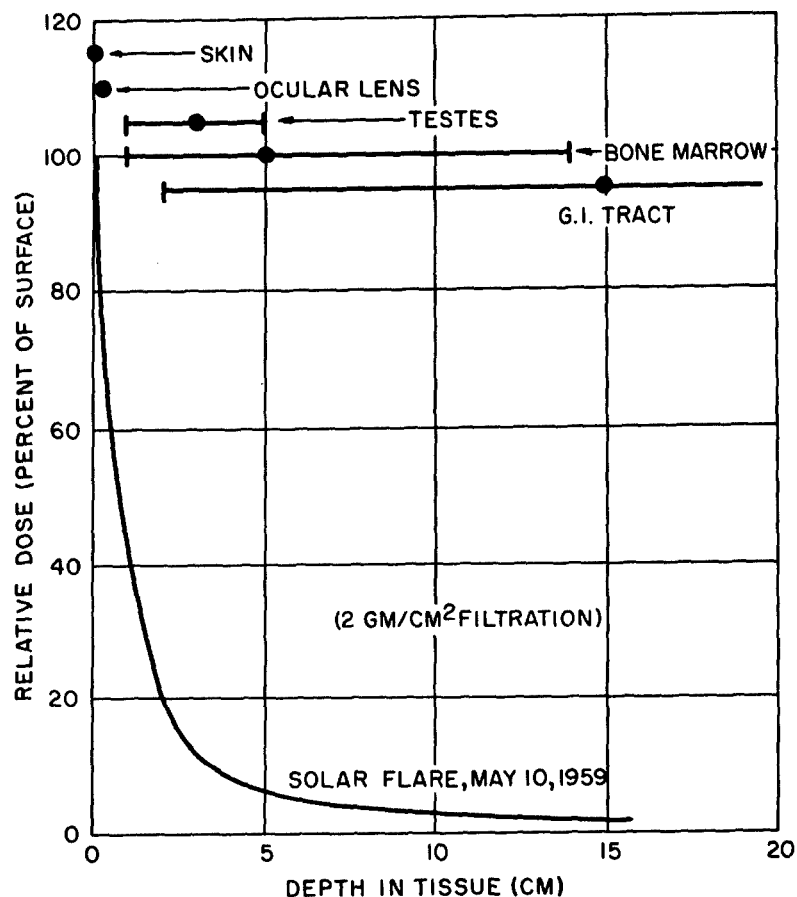


Figure 11.4 Depth range and mean depths of critical organs and tissues in relation to proton depth-dose distribution inside a spherical phantom placed behind 2 gm/cm<sup>2</sup> shielding, calculated for the May 12, 1959 solar event.

(After Langham et al, (65) drawn from Grahn (49) and Schaefer (95)).

of flares would probably not have been sufficient magnitudes to produce erythema of skin protected by spherical shielding equivalent to 2 to 5 gm/cm<sup>2</sup> aluminum shielding. Such shielding is thought to be representative of present day manned spacecraft hulls (1). On the other hand, at 1 gm/cm<sup>2</sup> aluminum, protraction and fractionation would probably not have been sufficient to prevent the occurrence of erythema (65).

In conclusion, an optimistic picture of the potential solar flare hazard to astronauts on prolonged space missions has been presented. It should

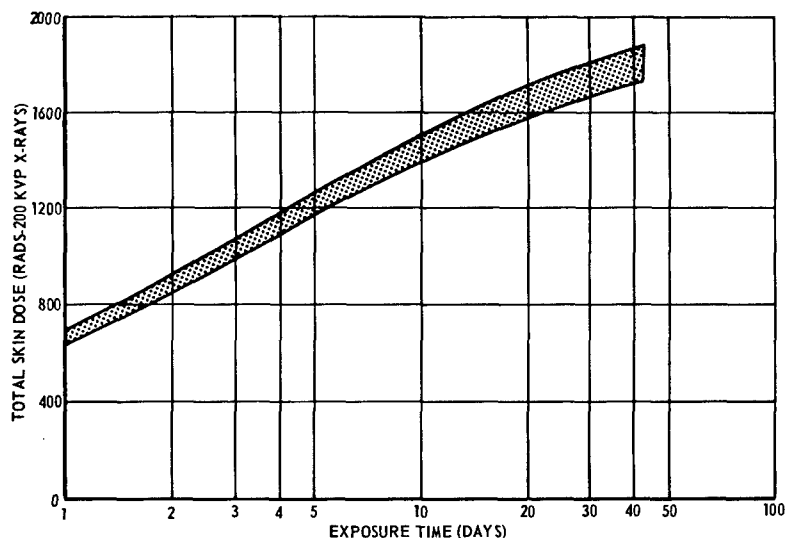


Figure 11.5 Total skin dose of 200 KVP x-rays, or a radiation with a QF of unity, required to produce a slight erythema as a function of time over which exposure is spread.

(After Langham et al (65)).

be remembered, however, that the above predictions were based on limited data from only one solar flare cycle. Accordingly, the treatment in space of various acute radiation effects, particularly skin injury, should be considered in emergency planning.

#### Acute Ionizing Radiation Effects

Studies of humans suffering from acute ionizing radiation effects following radiotherapeutic, nuclear reactor and nuclear bomb exposures have indicated that a stereotyped clinical picture of such effects, based on dosage alone, cannot be described (16, 24, 54, 65, 66, 79, 88, 101, 121). This applies even more so to radiation exposures in space. The different component particles and the energy-flux-time spectra of space radiations, with resulting variations in RBE and tissue depth-dose distributions of these radiations, are critical. These are only the major determinants of doses received by individual organs and tissues which, when damaged, are directly or indirectly responsible for producing the medical problems from radiation exposure.

The wide differences in species sensitivity to radiation is well known,



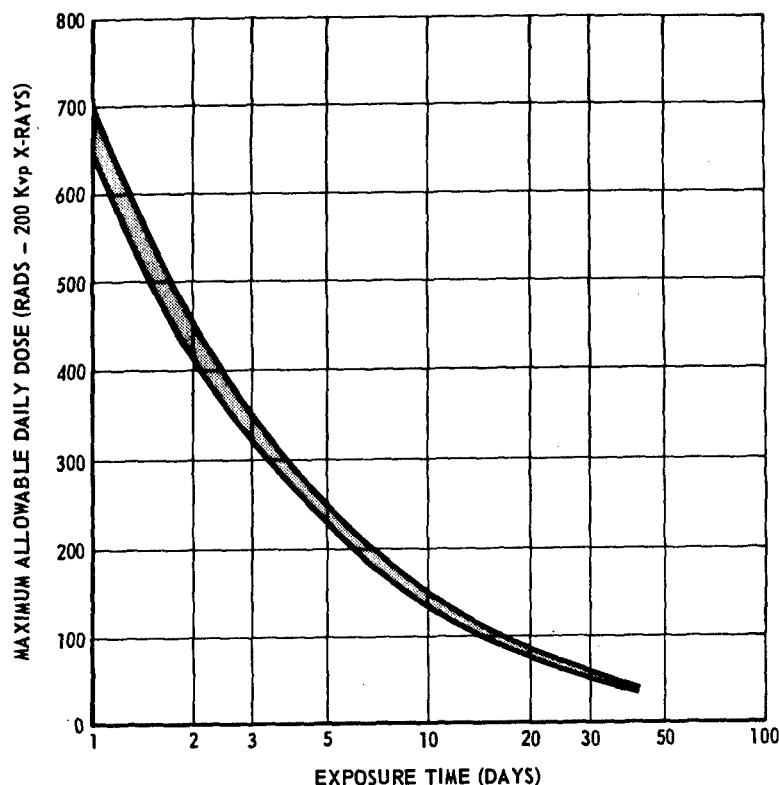


Figure 11.6 Maximum daily dose of 200 KVP x-rays, or a radiation with a QF of unity that can be given and not exceed the slight erythema threshold as a function of the period over which the exposure is protracted.

(After Langham *et al* <sup>(65)</sup>).

so that extrapolation of even subhuman primate radiation exposure data to man must be made with caution <sup>(13, 23, 32)</sup>. The effects of protons on animals have been studied and compared to the effects of other radiations <sup>(4, 15, 30, 31, 32, 33, 34, 61, 67, 103, 104, 105, 114)</sup>. In contrast to gamma or x-irradiation, studies of several species have indicated that for a total body dose, protons are more prone to damage the gastrointestinal tract than the bone marrow <sup>(30, 31, 32, 33, 34, 61, 67, 103, 114)</sup>. Early findings that hemorrhagic phenomena occur earlier and are more severe in large animals irradiated with protons than those irradiated with x-rays have not always been substantiated <sup>(31, 33, 83, 114)</sup>.

The clinical manifestations of early, or acute effects of a radiation exposure, tend to appear when the total dose of radiation absorbed by a

critical volume of tissue within a certain period of time exceeds some critical level, or threshold. For a single uncomplicated solar flare, this threshold will probably not be exceeded if signs and symptoms of radiation effects do not appear within 60 days after exposure to the flare <sup>(65)</sup>.

#### Clinical Picture Following a Highly Penetrating Exposure in the LD<sub>50</sub> Range

For the purpose of determining what therapeutic measures might be required for the treatment of acute radiation effects in space, a rather idealized clinical picture resulting from a total body dose of highly penetrating radiation given at a mid-lethal dose (LD<sub>50</sub>), such as 450 to 500 rads of 250 KVP x-rays, is described here <sup>(3, 14, 21, 24, 51, 65, 76)</sup>. What usually occurs at this dose level is the so-called hematopoietic form of the acute radiation syndrome. The clinical course of this form of reaction passes through four phases - the initial or prodromal phase, the latent phase, the bone marrow depression phase, and the recovery phase <sup>(3)</sup>. At lower dose levels, the bone marrow depression phase is less likely to become clinically apparent; symptoms characteristic of only the prodromal phase occur in about 5 to 10 percent of individuals receiving 50 to 100 rads, and in about 25 to 50 percent of those receiving 100 to 200 rads <sup>(61)</sup>. At levels above the LD<sub>50</sub>, evidence of gastrointestinal damage will appear. This so-called gastrointestinal form of the acute radiation syndrome, characterized by a severe prodromal phase, a short latent phase and a phase of usually fatal gastrointestinal disturbances, overshadows clinical manifestations from bone marrow depression at a total body dose in the range of 750 to 800 rads. As mentioned above, for a given total body dose, the human gastrointestinal tract might be more susceptible to proton injury than to injury from x-rays or gamma irradiation. The predominance of gastrointestinal injury might therefore occur at a somewhat lower dose after proton irradiation from a highly penetrating solar flare. At still higher total body radiation doses, the so-called cerebral form of the acute radiation syndrome appears, being characterized by an explosive initial phase followed by irrational behavior,

neuromuscular incoordination, convulsions and death within a few hours. Finally, it should be remembered that since depth-dose patterns are considerably different from those of the LD<sub>50</sub> x-ray model, the clinical manifestations resulting from doses between 450 and 500 rads from solar flares may also be quite different than those discussed below.

Initial, or Prodromal Phase - Anorexia, nausea, retching, vomiting, listlessness, apathy, increased fatigability and occasionally diarrhea usually begin within 2 hours after an acute radiation exposure in the LD<sub>50</sub> range (20, 43, 65, 79, 86, 88, 119). Weakness, fatigue, lethargy, and irritability, which have been attributed to the direct cerebral effects of radiation, may also become evident (98). Clinical experience indicates that the higher the integral dose, the shorter the latency of whatever prodromal symptoms occur. Signs and symptoms in the prodromal phase usually reach a peak within 4 to 6 hours after exposure, then improve rapidly, seldom lasting beyond 48 hours in duration.

The severity of clinical manifestations occurring in the prodromal phase correlates poorly with the integral dose of radiation received, being markedly influenced by individual susceptibility, which cannot be pre-determined, and by psychologic factors such as motivation (16, 65, 98). Some authors are of the opinion that the severity of nausea and vomiting might be proportional to the amount of food in the stomach at the time of injury, and may be prolonged by attempting to feed the irradiated individual (3). Symptoms might also be aggravated by fluid and electrolyte losses in vomiting.

It is readily apparent that the prodromal phase could be a threat to continued astronaut performance, especially if severe signs and symptoms occur during a crucial spacecraft maneuver. Vomiting into the weightless environment will also create a potentially disastrous droplet hazard (Chapter 8).

Latent Phase - The prodromal phase is usually followed by an asymptomatic period, or latent phase of up to several days in duration. Weakness

and fatigue can continue into this phase due to fluid and electrolyte losses from vomiting in the prodromal phase. Epilation usually occurs within two weeks, and involves mainly head and body hair, the eyelashes and eyebrows being less sensitive to radiation <sup>(3)</sup>. The duration of the latent phase is governed by the severity of the radiation exposure, and hence the damage incurred by the exposure.

Bone Marrow Depression Phase - Marked depression of circulating white blood cells, with associated failure of the body's immune mechanisms, leads to enhanced susceptibility to infection. Inflammation, with chills, fever and general malaise, is usually suffered first in the oropharyngeal region. Gingival and pharyngeal tissues, and tonsils can become severely swollen and ulcerated. Step-like fever suggests septicemia. A bacteremia can lead to abscess formation in any tissue of the body. Bacterial pneumonia and gastroenteritis can also be the cause of fatality.

Due to marked depression of circulating platelets, disturbance of blood clotting also becomes clinically evident. The gingival tissues bruise and bleed easily. Petechiae and ecchymoses may involve broad areas of skin. Gastrointestinal and urinary tract bleeding may also occur. Gross hemorrhage from body orifices and into hollow organs is, however, usually not massive and continuous, but is self limiting <sup>(3)</sup>.

In the average individual, clinical manifestations from an LD<sub>50</sub> dose of total body radiation usually reaches a peak about the fourth to fifth week after exposure. Death may occur primarily from infection or bleeding, or both.

Recovery Phase - The recovery phase is usually quite prolonged, lasting from 2 to several months in duration. Repeated infections, involving especially the respiratory system and skin, may occur. Bacterial resistance to available antibiotics can become a serious problem during this period.

#### Skin Manifestations

If the skin receives a radiation dose which is less than that required to

produce wet desquamation or ulceration, it will show a variable amount of flushing, or erythema <sup>(3)</sup>. This primary effect appears within hours, increases to a maximum intensity within 24 hours and disappears completely by the third day after exposure. There might be an accompanying sensation of warmth or itching resembling a mild sunburn. About 10 to 15 days after exposure, the skin again becomes erythematous, this time more intensely than the more fleeting early erythema. The involved skin in this so-called main erythema phase, which usually lasts about 2 weeks in duration, gives symptoms of a severe sunburn. Depending on the body sites and surface areas involved, it is readily apparent that an astronaut could be markedly impaired during this phase, especially if affected sites must be in contact with tight-fitting or potentially chafing parts of a space suit.

With larger doses of radiation, the skin may develop a bluish-red color with superficial scaling (dry desquamation) or a more severe reaction with blisters (moist desquamation). These extremely irritating, painful conditions usually develop by the ninth day after exposure. Severe toxicity and the serious sequelae of plasma protein, fluid and electrolyte losses can become part of the clinical picture if a large area of the body surface is involved with blistering. After still larger doses of radiation, blisters may ulcerate to form so-called roentgen ulcers over a period of several weeks <sup>(3)</sup>. These extremely painful, slow healing ulcers are characterized by marked pain, a punched out appearance, undermining growth and a tendency to recur <sup>(3)</sup>. Any areas of skin breakdown are markedly prone to become infected. It is noted that the clinical course of primates dying from proton radiation injury to skin is in many ways similar to that following third degree thermal burns (Chapter 13) <sup>(27, 29)</sup>. A severe, persistent edema, which often progresses to fibrosis or necrosis, can develop under severely irradiated skin from many weeks to many months after exposure <sup>(50)</sup>. This delayed phenomenon has been well demonstrated in primates whose skin was irradiated with high doses of 32 Mev protons, and is thought to be due to increased capillary permeability in conjunction with a moderate hypoalbuminemia <sup>(27, 29)</sup>. Severe subcutaneous fibrosis with contracture

and decreased mobility often leads to slow starvation death in these primates.

The effect of radiation on the skin varies, depending on the RBE of the radiation, on the degree of protraction or fractionation of the dose, on the site exposed, and probably on the surface area exposed. Reference is again made to data depicting the effect of dose protraction and fractionation on the production of skin erythema, presented in Figures 11.5 and 11.6. In general, the threshold dose at a depth of 1 mm for a slight erythema is about 650 to 700 rads of rapidly administered 200 KVP x-rays (59, 65). After an acute exposure with 200 KVP x-rays, a sharp erythema is seen about 1050 rads and a blistering reaction about 2000 rads.

#### Diagnosis

For the most part, the diagnosis of acute radiation effects, especially skin injury, should be easily made in space. Measurement of the energy-flux-time characteristics of a radiation exposure and subsequent estimation, especially of tissue dose received by an astronaut over a period of time should, based on prior human and animal studies, allow reasonably accurate prediction of clinical outcome. Hopefully the time sequence and characteristics of acute radiation effects will not have to be relied upon as the first warning of radiation exposure. Whenever possible on board future spacecraft, hematologic studies, such as total and differential white cell count, and hemoglobin and hematocrit determination, to assess the degree of hematopoietic depression or secondary blood loss, could be a valuable aid for therapeutic decisions and prognosis. As well, fluid and electrolyte studies might be indicated for assessing the degree of fluid and electrolyte imbalance resulting from a radiation exposure, and for accurately determining the required replacement therapy.

#### Prevention

The importance of minimizing the amount of radiation which an astronaut receives by the use of adequate shielding and, whenever possible, by controlling the duration of his exposure, has been emphasized. For

necessary exposures, daily fractionation in equal exposure increments would be simpler and preferred, so that the limits within which an exposed astronaut can operate without decrement in health or performance can be predicted <sup>(68)</sup>. Radiation dose limits currently recommended by the National Aeronautics and Space Administration are listed in Table 11.2. The models of man on which these standards were based are presented elsewhere <sup>(44)</sup>. It has been stated that these maximum permissible doses are probably on the conservative side when one takes into consideration the effect such doses would have on astronaut performance and consequently on the safety of a mission <sup>(9)</sup>. For example, fatal mistakes might be made if a radiation prodromal reaction peak should occur in one or more crew members when some critical maneuver such as rendezvous and docking, or a mid-course trajectory correction would be required. On the other hand, this peak might occur over a period when only a minimum amount of crew activity would be required. The mission plan could then be altered so that this period could be pro-

Critical organ	Maximum permissible integrated dose (rem)	RBE (rem/rad)	Average yearly dose (rad)	Maximum permissible single acute emergency exposure, protons only (rad)	Maximum permissible single acute emergency exposure, alpha particles and protons (rem)
Skin of whole body	1600	1.4 (approx)	250	500*	700*
Blood-forming tissues	270	1.0	55	200	200
Feet, ankles, and hands	4000	1.4	550	700**	980**
Eyes	270	2***	27	100	200

\* Based on skin erythema level.

\*\* Based on skin erythema level; however, these appendages are believed to be less radiosensitive.

\*\*\* Slightly higher RBE assumed since eyes are believed more radiosensitive.

Table 11.2 Radiation exposure dose limits currently recommended by the National Aeronautics and Space Administration.

(After Gill <sup>(35)</sup>, National Academy of Sciences Space Science Board <sup>(59)</sup>, and Billingham <sup>(8)</sup>).

longed enough to allow recovery. Finally, it should be pointed out that one important change was made in the original radiation exposure limits table established by the National Academy of Sciences Space Science Board <sup>(84)</sup>. Pointing out that alpha particles may be present in greater numbers in large solar flares than originally predicted, Billingham <sup>(9)</sup> suggested that it was more logical to specify biologic limits in terms of rem since the alpha particles encountered during space missions would probably have an RBE greater than 1. Although penetration of the space suit by solar "wind" alpha particles will be so small that these particles will have essentially no biologic effectiveness, alpha particles from high energy solar flares could, on the other hand, present a significant hazard to occupants of spacecraft, especially if shielding is minimal <sup>(22, 96)</sup>.

If there is a significant risk of an astronaut being exposed to levels of radiation dosage above those in Table 11.2 or its future modifications, it will be necessary to have him take special protective measures. This is based on the fact that increasing the shielding incorporated in a spacecraft hull or providing a highly shielded compartment in a spacecraft might not be possible in the light of the great weight penalties these measures impose. Optimum cabin shielding should be provided by distributing on-board systems and stores to keep the doses to critical organs to a minimum. Since estimated doses received from solar flares tend to vary considerably in different parts of space cabins, an astronaut may be able to take up a "safer" position in the cabin during a solar flare. The early high-energy component of a flare is essentially unidirectional in space <sup>(73)</sup>. Orienting the spacecraft in the direction of the arriving flux could therefore be an effective protective measure. Appropriate distribution of moveable on-board equipment and stores might add to the directional shielding effect. In an emergency situation it might be found necessary to provide an astronaut with local shielding which could be placed over critical areas of his body, such as eyes, thorax or abdomen. Lastly, the space suit should be designed to provide adequate shielding during extravehicular operations, or the durations of such



operations carefully controlled to protect an astronaut, especially from skin injury.

Several recent reviews have indicated that there is no radio-protective drug with a therapeutic index suitable for human use at the present time (6, 7, 58, 65, 89, 93, 99, 100, 112, 115). Although hundreds of chemical compounds have been shown to have some radio-protective effect in mammals, marked species variability, especially with respect to toxicity, has prevented extrapolation of results with such compounds to man (35, 37, 38, 58, 65, 69, 85, 93, 100, 112, 115, 119). Furthermore, no data are available on the single or combined use of such drugs on humans.

A rather "shotgun" approach to drug studies has evolved from a failure to define the exact mechanism of radiation injury. Current thought supports simultaneous action of radiation on critical biologic molecules through direct hit phenomena and harmful secondary reactions of chemically reactive ions and radicals with critical sites on molecules. Free radicals are created mainly by the action of radiation on the abundant intra- and extracellular water. Apparently by scavenging free radicals, compounds consisting of a free sulfhydryl group separated by not more than 3 carbon atoms (e.g., cysteine, glutathione, cysteamine, AET or aminoethylisothiurea, MEA or mercaptoethylguanidine) have, especially in the light of their relatively low toxicity, been the more effective radiotherapeutic agents in animal studies (35, 37, 58, 65, 69, 77, 93, 100, 112). Other antioxidants (e.g., ascorbic acid, BHT or butylated hydroxytoluene) have been particularly effective in the rat (38). Possibly on the same basis, various natural food substances (e.g., alfalfa, broccoli, vitamin mixtures) have been mildly effective in the guinea pig (85). The radioprotective effect of drugs such as 5-hydroxytryptamine, histamine, and epinephrine has been attributed to the lowering of tissue oxygen, an increased amount of which appears to enhance the production of these harmful radicals (65, 112). Several investigators have recently found that for some unknown reason, dimethylsulfoxide (DMSO), which has remarkably low systemic toxicity in both animals and humans, exerts a radioprotective effect in animals (5, 39, 63, 81, 91). Since this agent

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has a high penetrating power through intact skin and promotes the cutaneous penetration of certain drugs, the question is raised as to whether or not it alone or in combination with another radioprotective agent might give not only systemic, but also selective dermatologic protection from radiation when applied topically (63, 108, 109).

The toxicity and rapid detoxification or metabolic breakdown of almost all radioprotective drugs and the extreme rapidity of ion and free radical formation in the tissues have dictated that virtually all of these drugs be administered just prior to exposure (35, 58, 65, 112). Analysis of the energy-flux relationships in early stages of a flare may allow prediction of organ-specific doses during the remainder of the flare and the subsequent potential value of radioprotective drugs.

An adequate tissue level of the prophylactic agent must be maintained during the anticipated exposure. At the present time, the low therapeutic index of radioprotective drugs renders their use in space impractical. Toxicity might be adequately reduced, however, by using combinations of these drugs, each in a lower dosage. It cannot be overstressed that the potential hazard presented by a radiation exposure must always be weighed against the potential toxicity of the radioprotective drug in the light of maintaining optimum astronaut efficiency and assuring mission success.

Finally, since skin injury appears to be the most likely radiation effect beyond prodromal reactions to occur in space, one might suggest the development of a radioprotective agent which would selectively fix in the skin. Such drugs would require freedom from local and systemic toxicity to make their use in space practicable. It is also hoped that skin fixation may reduce the systemic component which is currently the limiting factor in the use of radioprotective agents.

### Treatment

From past experience with acute effects of radiation on humans, it would, in general, seem best to treat in space clinical manifestations from radiation exposure as they arise, providing symptomatic therapy as dictated by sound clinical judgment (17, 21, 57, 65, 74, 76, 106).

This is due to the fact that many acute radiation effects are non-specific, so that therapeutic measures are directed mainly at signs and symptoms, such as nausea and vomiting, and infection.

Many drugs, given both orally and systemically, have been used to treat especially nausea and vomiting in the prodromal phase of the acute radiation sickness syndrome (19, 55, 60, 64, 70, 102, 110, 111, 118). Assessment of their effectiveness is difficult, however, due to the lack of well controlled clinical studies, ignorance of the precise etiologic mechanisms involved in the prodromal phase, and the fact that psychogenic overlay in tense, nervous individuals, especially those already suffering from unrelated illness, undoubtedly influences response to such drugs (16, 64, 111). Vitamins of the B complex, particularly pyridoxine, were the first agents with reported effectiveness, and are still widely used (102, 111, 118). Although antihistamines, such as cyclizine hydrochloride and diphenhydramine, have proven useful for motion sickness, they have not successfully controlled clinical manifestations in the prodromal phase (110, 111). In the past few years, phenothiazine derivatives, such as chlorpromazine, prochlorperazine thiopropazate, fluopromazine, pecazine, trifluoperazine and triethylperazine have been tried extensively and found to be more effective than all other drugs (19, 55, 60, 70, 110, 111). Of these tranquilizing agents, triethylperazine has shown the greatest promise for the control of nausea and vomiting in the prodromal phase (19, 55, 60). This drug, which appears to sedate both the chemoreceptor trigger zone and the vomiting center, is relatively free of side effects (19, 55, 60, 64). Further substantiation of the drug's effectiveness is still required. Finally, in the light of the lack of overwhelming success of any drug in controlling clinical manifestations in the prodromal phase, this area demands intensive investigation.

If a drug is available in space for the prodromal phase it might be given prophylactically to an astronaut who has received a high dose of radiation. In this respect, one must keep in mind the dangerous situation

which will result if an astronaut vomits into the weightless environment (Chapter 8).

Diarrhea following radiation exposure might be controlled with an antidiarrheal drug, such as methscopolamine bromide or diphenoxylate hydrochloride. The administration of an intravenous electrolyte solution, such as Ringer's lactate solution, might be indicated for the restoration or maintenance of fluid and electrolyte balance. Any infection must be treated with an appropriate broad spectrum antibiotic.

No specific treatment of radiation injury of the skin has evolved from past experience in this area. Artz <sup>(3)</sup> recommends application of a bland ointment, protection of lesions from further trauma and air with large bulky dressings, and relief of associated discomfort with an analgesic. Topical anesthetics are apparently ineffective in controlling pain. Radiation lesions would then be managed in space in a manner similar to that described for thermal burns in Chapter 13.

Recently, attempts have been made to modify the skin reaction to radiation with topical and oral cortisone preparations (11, 56, 62, 71, 82, 113). Results, however, have been equivocal. There may be some suppression of the early erythema and some delay in the onset and initial severity of the main erythema phase, but the degree of skin damage eventually incurred by radiation has not been significantly altered by these preparations. Pertinent to an astronaut's performance following a severe skin dose of radiation is the fact that it has not been noted whether or not cortisone agents can reduce discomfort associated with the early and main erythema phases.

As previously mentioned, a significant risk of damage to an astronaut's bone marrow by solar flares in space cannot be definitely established from data to date. Accordingly, a requirement for transfusions of blood elements (e.g., red blood cell, white blood cell or platelet concentrates) or bone marrow transplants in space, cannot be predicted. If the need for such measures is indicated by future assessments of space radiation hazards, the cryogenic storage of blood cell concentrates and homologous

or autogenous bone marrow should be considered (2, 8, 12, 75, 76, 78, 107). It is hoped that rapid advances in this technology could make such an approach feasible for space operations.

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## CHAPTER 12

### INJURIES FROM METEOROID PENETRATION

Knowledge to date has indicated that the probability of penetration of a spacecraft cabin wall or space suit by a meteoroid during missions along relatively meteoroid-free routes in space is quite low (12, 45, 52). Uncertainties still remain, however, for a great deal more data is required on the frequency, density and frangibility of meteoroids, and on the particle characteristics for penetration of various spacecraft wall and space suit materials. Accordingly, it is apparent that in the face of current optimism, attention must still be given to the possibility of having to treat in space any one or more of a number of injuries which could result from the primary (flash, heat, blast, projectiles) or secondary (e.g., decompression, fire, electrical disruption) effects of meteoroid penetration. This chapter briefly discusses the meteoroid hazard, and the characteristics, diagnosis and treatment of injuries thought possible from meteoroid penetration of the spacecraft cabin wall and space suit.

#### Meteoroid Hazard

Current information on the meteoroid environment in space can be obtained from the studies of Cosby and Lyle (12) and others (7, 15, 22, 28, 45, 50, 52, 53). The word "meteoroid" is a general term applied to particles of matter traveling in space. Ninety percent of meteoroids are presumably of cometary origin; the remainder are of asteroidal origin (50). Seventy percent apparently travel in random directions through space; the remainder travel in streams (45). The majority of meteoroids are thought to be highly porous and frangible with densities as low as  $0.5 \text{ gm/cm}^3$  (cometary meteoroids) (28, 37). A few denser meteoroids have predicted densities of up to  $9 \text{ gm/cm}^3$  (asteroidal meteoroids) (22). The geocentric velocity of meteoroids apparently varies from 11 to 72 Km/sec (28).

Since the Earth passes through streams of meteoroids traveling in heliocentric orbits, the meteoroid flux in the near-Earth environment varies at regular intervals during the calendar year. This flux is highest

in the summer months (May through October) and lowest during the late winter months (January through April) <sup>(7)</sup>. The various known meteoroid streams and their orbits have been discussed by Burbank and Cour-Palais <sup>(7)</sup>. Such information could prove quite valuable in mission planning, especially if potentially penetrating particles are present in these streams.

The best data to date on the probability of meteoroid penetration of various thicknesses of aluminum are summarized graphically in Figure 12.1. The best estimate curve shows that for a spherical shell 3 meters in diameter, penetration of an 0.03 cm thick aluminum wall would occur on the average of about every 2.3 years. There is, however, a level of uncertainty of about one order of magnitude surrounding this and other estimates of the penetration hazard <sup>(45)</sup>. Additional data, especially on meteoroid density and frangibility, are needed to establish more accurate estimates.

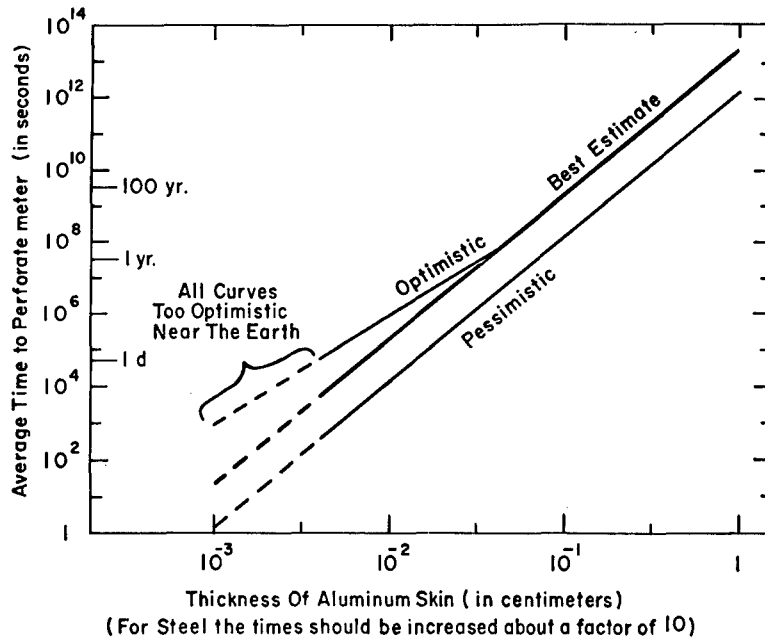


Figure 12.1 Time to meteoroid perforation of a spherical thin metal shell 3 meters in diameter (28 square meters in surface area).

(After Whipple <sup>(52)</sup>).

## Injuries From Meteoroid Penetration of a Spacecraft Cabin Wall

Events and associated injuries from meteoroid penetration of a spacecraft wall have been described by Roth <sup>(45)</sup>. Pertinent to his considerations were various ground-based studies simulating penetration conditions (23, 33).

Meteoroid penetration of the spacecraft cabin wall might be partial or complete. A partial penetration might cause injuries if particles spall, or chip off the inner surface of the wall. If complete penetration occurs, vaporized molten and hot, fragmented, meteoroid and wall materials will be ejected into the cabin. The vaporized materials will immediately undergo "explosive oxidation", and hence constitute a flash, burn and blast hazard. Molten and hot fragmented materials could travel at high velocities, mechanically injuring an exposed astronaut and damaging equipment. Finally, fragmented meteoroid and wall could penetrate containers, disrupt tubes and pipes, and even cut electrical wires, thereby markedly increasing the fire hazard.

The probability of meteoroid penetration of a spacecraft cabin wall can be reduced by placing penetration barriers around the whole spacecraft or over critical areas of its hull. The most effective barrier appears to be a so-called "bumper shield" which fragments or disperses the meteoroid. A core material can be placed under the shield to accept the momentum of the fragmented and molten meteoroid and shield before these materials reach and damage the spacecraft cabin wall. Further design measures in meteoroid protection are discussed below.

Possible injuries due to the primary phenomena (flash, heat, blast, projectiles) associated with meteoroid penetration of a spacecraft cabin wall are discussed below. It must be kept in mind, however, that the severity of injury and consequent functional impairment of an exposed astronaut will also depend on the magnitude of secondary effects of penetration. Explosive decompression injuries (Chapter 3), acute hypoxia (Chapter 1) and ebullism (Chapter 2) might occur. The magnitude of the decompression hazard will depend on the size of the hole a meteoroid

makes in the cabin wall, the cabin volume, the initial cabin atmospheric pressure and emergency recompression and patching capabilities. There might also be risks of thermal, electrical and chemical burns from fires, disruption of electronic circuitry, and release of chemicals from life support and analytical systems (Chapter 13). Any one or more of a great variety of clinical problems might also result from the release of hazardous particles and droplets into the spacecraft cabin atmosphere (Chapter 8).

### Light (Flash) Injury

The "oxidative explosion" of the vaporized meteoroid and spacecraft cabin wall materials will produce a flash which will probably last on the order of 1 millisecond <sup>(23)</sup>. The intensity of this flash will depend on the magnitude of the penetration, the composition of the wall, and the composition and pressure of the cabin atmosphere. Titanium alloys produce more severe flashes in 100 percent oxygen environments than do aluminum alloys <sup>(33)</sup>. The peak flash intensity is markedly increased in pure oxygen as compared to air, especially at an atmospheric pressure of 5 psia <sup>(23)</sup>.

The flash associated with meteoroid penetration of a spacecraft cabin wall might produce either transient (flashblindness) or permanent (chorioretinal burn) visual impairment of an exposed astronaut. Factors influencing the degree of this impairment include the proximity of the eye to the site of penetration, the direction of gaze, the reflective properties of surfaces, and level of illuminance in the cabin and the size of pupil at the moment of the flash. A recent review has summarized current knowledge in this area <sup>(59)</sup>.

Chorioretinal burns produce permanent blindness. The chorioretinal burn threshold for the dilated human eye has been estimated to be about 240,000 lumens/ft<sup>2</sup> <sup>(34)</sup>. In a simulated meteoroid penetration study, hypervelocity particles passing through aluminum targets into a 100 percent oxygen atmosphere at sea level pressure and at 5 psia produced light flashes as high as 273,000 lumens/ft<sup>2</sup> <sup>(23)</sup>. This value was reduced by 85 percent when the flash occurred in air at sea level pressure and in a 50 percent oxygen-nitrogen atmosphere at a pressure of 7.0 psia. Hence the concentration of oxygen in the spacecraft cabin atmosphere

could markedly influence the risk of blindness from meteoroid penetration of a spacecraft cabin wall. From these considerations, it appears that this risk will be low unless an astronaut is in a high oxygen environment and is in close proximity to the site of penetration. On the other hand, a varying degree of flashblindness is considered highly probable. Further study in this area is warranted, however.

Flashblindness is a transient reduction of visual acuity due to bleaching of visual pigment by a flash of light. The blind area usually occupies the central field of vision, so that useful vision is temporarily lost. The data of Severin and co-workers (21, 48) indicate that the recovery time of flashblindness probably varies between 6 and 48 seconds in the 100,000 to 240,000 lumens/ft<sup>2</sup> flash exposure range. The marked effect an increase in visual field illumination has in reducing visual recovery time has been demonstrated (26, 34, 48).

Various specific measures can be suggested for the protection of an astronaut's eyes from meteoroid flash, especially if a potentially hazardous meteoroid flux is predicted or encountered during a space mission. So-called "fixed filter" goggles use a selected filter of fixed density to absorb or reflect radiant energy before it enters the eye. Since these goggles would have to be worn continuously during high risk situations, there would have to be a compromise between the degree of filter opacity required for protection and the transmission necessary for adequate vision.

The monocular eye patch is simple and reliable, but has some obvious drawbacks (29). Stereoscopic vision is lost and the visual field is restricted. If the exposed eye is injured, the covered eye would become the sole visual resource of the astronaut (59).

The effectiveness of "peep-hole" or eye slit shields is based on the fact that by reducing the angle of vision, the chance of a flash of light being directly focused on the retina is reduced (59). The obvious limitation to this technique is restriction of the visual field. A variation of the eye-slit technique is the use of a visor, screen, of bilateral blinders to restrict the field of vision. Again, these measures would be effective

only if a flash occurred outside of the momentary field of view.

The most desirable all-around protective system would be clear eye shields impregnated with a phototropic substance which is darkened by intense light <sup>(59)</sup>. To be effective in a meteoroid penetration situation, the photochemical reaction time would probably have to be considerably less than 1 millisecond <sup>(33)</sup>. Various types of photoreactive devices are described in the literature <sup>(1, 20, 59)</sup>.

A drug-induced miosis could serve to prevent chorioretinal burns and reduce the duration of flashblindness. Experiments have indicated that a pilot can perform instrument readings under minimum instrument illumination while his pupils are constricted, that eye discomfort from ciliary spasm was not a significant side-effect of this measure, and that based on the laws of optics, the limitation of light entering the eye should afford chorioretinal burn protection and minimize the duration of flashblindness <sup>(35)</sup>. However the potential usefulness of a miotic drug in a high risk space situation will require a complete assessment, especially with respect to visual-motor task performance under induced miosis in the simulated spacecraft environment.

There is no definitive therapy for either chorioretinal burn or flashblindness <sup>(34, 48)</sup>.

### Burns

Since the flash of "explosive oxidation" extended only a few inches into model spacecraft cabins in simulated meteoroid penetration studies, it is considered likely that the "explosive oxidation" produced by a smaller penetrating meteoroid particle in space will be highly localized in the spacecraft cabin <sup>(23)</sup>. Even so, there will be a risk of an exposed astronaut suffering a local burn if he is in close proximity to or in direct contact with the "explosive oxidation". Respiratory tract damage from the inhalation of hot gases and noxious fumes is also considered possible. Molten and hot meteoroid and wall materials ejected into the cabin could produce multiple small burns on body areas in direct line with the movement of these materials. Involvement of the eyes, especially corneal burns, could be extremely incapacitating. It should also be remembered

that these missiles could compound the risk of burns by starting fires in the spacecraft cabin.

Burns in general are discussed in Chapter 13. The treatment of corneal injuries is covered in Chapter 8.

### Blast Injuries

The "explosive oxidation" of vaporized meteoroid and spacecraft cabin wall materials will not only produce a flash and a local increase in temperature, but also a local increase in pressure which will be rapidly propagated throughout the cabin. The blast hazard based on a comparison of findings in simulated meteoroid penetration studies with estimated pressure-duration relationships required for 50 percent lethality of adult humans has been assessed <sup>(45)</sup>. However, even though it was concluded that spacecraft penetrations of magnitudes similar to these studies would not cause lethal blast injuries to an astronaut sitting in the center of a 100 cubic foot cabin, many specific factors which are yet to be assessed could greatly modify this hazard. Some of these factors are pointed out below. One should also keep in mind that explosions in the cabin from other causes would produce injuries similar to those from a meteoroid blast.

The physics, biophysics, and pathophysiologic and clinical consequences of blast have been well documented in the literature. Excellent reviews written by Clemenson <sup>(11)</sup>, White and co-workers <sup>(5, 13, 39, 56, 57, 58)</sup>, Chiffelle <sup>(10)</sup> and others <sup>(14, 18, 30, 41, 45, 49)</sup> make it unnecessary to discuss this area in detail here. It is important to note, however, that even though a great deal of information has been obtained from the exposures of man and animals to bombs and other sources of blast, much is to be learned of the possible biologic consequences of blast in the closed cabin situation, particularly under conditions of lowered ambient atmospheric pressure and altered atmospheric pressure and gas composition.

The overpressure or "shock" wave of an explosion spreads out radially from its source. Peak overpressure (pressure above ambient atmospheric

pressure) and time-integral of overpressure (impulse) decrease exponentially, so that its injurious power is rapidly lost. The rising phase of a pressure wave hitting a target is steep unless propagation is slowed, as for example, by the interposition of barriers between the source and target. Extremely pertinent to considerations of explosions occurring in a confined volume such as a spacecraft cabin is the fact that pressure reflections occur when a blast wave impinges on a solid object. The magnitude of focused and reinforced reflection can be two to nine times greater than the incident pressure <sup>(58)</sup>. Hence, depending on such factors as the site of meteoroid penetration, the geometry of the cabin, the pressure reflective and absorptive properties of the cabin walls, and his position in the spacecraft cabin, an astronaut could be exposed to a steep, step-wise, injurious pressure loading from an otherwise non-injurious incident pressure pulse. The underpressure (pressure less than ambient atmospheric pressure) which usually follows the passage of a blast-produced overpressure will probably be reduced in a spacecraft cabin explosion by reflected pressure waves. The role which rapid or "explosive" decompression could play in altering the meteoroid blast hazard has apparently not been determined. Translational wind loading from a meteoroid blast should not be of a significant magnitude to cause injuries by imparting movement to an astronaut or by creating missiles of disrupted cabin structures. On the other hand, such traumatic events could result from associated rapid or "explosive" decompression (Chapter 3).

The amount of bodily injury an individual exposed to a blast overpressure will suffer is determined mainly by the rate of rise, magnitude and duration of the overpressure <sup>(5, 39, 55, 57)</sup>. The blast hazard in a closed environment such as a spacecraft cabin will probably be modified to a great degree by the step-wise characteristics of the overpressure rise, the atmospheric pressure, and the position and orientation of the individual to the incident pressure wave and reflecting surfaces <sup>(55)</sup>. Simulated meteoroid penetrations indicate that blast injuries following a meteoroid penetration in space will be due to extremely fast-rising



overpressures of short duration <sup>(23)</sup>. However, no simulations of penetration of large cabins have been performed.

Tissue damage from the absorption and passage of a blast wave through the body appears most commonly where density gradients of interfaces between tissue components are greatest <sup>(10)</sup>; however, it is considered possible that some tearing of tissues can result from shear stresses produced by acceleration of adjacent tissues of different densities <sup>(11)</sup>. Hence most blast pathology is seen within or in close proximity to air and gas-containing organs, such as the tympanic membranes, lungs, gastrointestinal tract and paranasal sinuses.

Which of many proposed mechanisms is the primary one in producing the tissue-air interface type of injury cannot be stated, however <sup>(9)</sup>. Passage of a pressure wave across such a sharp density interface appears to have a bursting or shredding effect on tissues, but whether spallation actually occurs is not clear <sup>(11)</sup>. It might even be possible that the heat associated with bubble compression might be damaging <sup>(9)</sup>. Disruption of blood vessels might be caused by the forced displacement of blood due to inadequate equalization of pressures in internal body spaces with blast overpressures <sup>(58)</sup>. Air might even be forced into the circulation when the pressure pulse reaches air spaces into which vessels have ruptured.

Pure air blast injury is characterized by lesions in various internal organs without any signs of external injury <sup>(11)</sup>. The tympanic membranes are the structures most vulnerable to shock waves <sup>(30, 55)</sup>. In fact, the threshold for disruption is thought to be about 5 psia for fast-rising overpressures. Tympanic membrane disruption with or without dislocation of the ossicles is common, especially when the rise of overpressure is steep <sup>(30)</sup>. Structural damage of the organ of Corti can also result from violent inward displacement of the membrane-ossicular system.

The more serious pathophysiologic effects of blast are predominantly attributable to damage to pulmonary tissues. The major determinant of survival in the immediate post-exposure period is the amount of air which enters the vascular system through disrupted pulmonary and

bronchial veins, and capillaries at the time of blast and subsequently with each respiratory cycle <sup>(58)</sup>. Although it is not definitely known over how long a period this phenomenon can occur, the early steep portions of time-mortality curves of animals exposed to blast overpressures indicate that most air entry takes place within 30 minutes from the time of blast <sup>(45, 46)</sup>. Reflex vasoconstriction and blood clotting tend to stop air from entering the pulmonary circulation. Aggravating this embolization are coughing, partially obstructed airways, left cardiac decompensation and the ill-advised use of positive pressure breathing in treatment. There is no clear correlation between the degree of pulmonary hemorrhage and the occurrence of air embolism <sup>(10)</sup>. The air which enters the pulmonary venous system embolizes to the left heart, and thence to the systemic arterial system. By producing local ischemia in such vital tissues as the brain, spinal cord, and heart, these bubbles can cause a great variety of mild to serious, temporary or permanent clinical manifestations.

Air can also pass through disrupted alveolar walls into peribronchial tissues. It can dissect through these tissues into the hilum of the lung and even up into the subcutaneous tissues of the neck and face. In the mediastinum, air can exert pressure on large central vessels, restricting blood flow through them <sup>(24)</sup>. This serious consequence of mediastinal emphysema is considered unlikely except in extremely severe cases, however <sup>(9)</sup>.

A blast wave can also produce a frank laceration of a lung leading to hemorrhage and the passage of air into the pleural cavity <sup>(11)</sup>. A torn pleural flap can have a flutter valve effect, allowing air to enter but not leave the pleural cavity. The resulting so-called "tension" pneumothorax can lead to severe cardio-respiratory embarrassment and a potentially fatal situation within minutes.

If an individual survives the initial effects of a severe blast, he might be faced with severe respiratory embarrassment due to pulmonary hemorrhage and edema. A bacterial pneumonia is also more likely to occur in a severely damaged lung <sup>(9)</sup>. An irreversible consequence of blast injury of the lung is chronic respiratory embarrassment from severe

alveolar disruption and subsequent patchy fibrosis of pulmonary tissue (11, 55).

Gastrointestinal hemorrhage and perforation can be produced by shock waves striking the body (11, 58). Ensuing contamination of the peritoneal cavity can lead to fatal peritonitis. Yet another tissue-air effect of blast overpressures is bleeding from the paranasal sinuses.

Contusion of the heart, often associated with disruption of papillary muscles and chordae tendinae, has been observed in individuals exposed to severe blast overpressures (58). Liver and splenic hematomas and lacerations can also result from blast, presumably due to tissue shearing effects.

It is readily apparent that many causes of "shock" and death are possible following blast exposure. Other than the organ injuries completely incompatible with life, such as cardiac rupture, massive air embolization to the brain and heart appears to cause the majority of blast fatalities in the early post-exposure period. Asphyxia from pulmonary hemorrhage and edema, and cardiac decompensation due to myocardial ischemia can occur from minutes to days following blast. Pneumonia and peritonitis could lead to "shock" and death over a period of many hours to several days.

The clinical manifestations of blast trauma are extremely variable. An individual can be killed outright without external signs of injury, although blood-tinged froth or frank blood often appears in the nose and mouth. Survivors frequently suffer from air hunger, with rapid shallow respirations, and are usually quiet, apathetic or even lethargic for a period of time (10).

A marked reflex bradycardia, probably from the stimulation of stretch receptors in the carotic sinus and lungs by the pressure pulse, can cause an immediate profound hypotension which might be severe enough to produce faintness or loss of consciousness (10, 11). In moderate blast injuries, systemic arterial pressure may recover slowly over a period of several days (11).

A period of apnea, lasting several seconds to more than a minute in

duration usually follows exposure to a shock wave. If the lungs are severely injured by blast, breathing may be slow, shallow and weary, often with extreme expiratory dyspnea <sup>(11)</sup>. Panting respiration in other cases is usually associated with complaints of tightness across the chest and varying degrees of chest or abdominal pain. Coughing will occur, but not usually early <sup>(10)</sup>. Hemoptysis may appear, often well within an hour, and tends to be repeated <sup>(10)</sup>. Epistaxis may occur from nasal sinus hemorrhage. Frothy blood coming from the mouth and nose is usually a bad prognostic sign <sup>(11)</sup>. Physical exertion tends to aggravate pulmonary bleeding, hence giving strong support for early and complete immobilization of an individual injured by blast <sup>(10)</sup>. Severe lung damage, or cardiac damage, and secondary pulmonary edema can lead to cyanosis and "shock" from impaired ventilatory function.

Any number of clinical manifestations due to focal or diffuse damage of the central nervous system by air emboli can occur. These include unconsciousness, convulsions, general and local paralyses and disturbances in equilibrium. Myocardial ischemia produced by bubble emboli or secondary to contusion can produce anginal pain, fatal cardiac arrhythmias and myocardial insufficiency leading to pulmonary edema, extreme dyspnea, cyanosis, "shock" and death. Less massive air embolization may simply cause temporary chest or abdominal pain <sup>(58)</sup>.

A large pneumothorax, particularly of the "tension" variety, can produce cardiorespiratory embarrassment characterized by severe chest pain, dyspnea, hemoptysis, cyanosis and "shock". Mediastinal emphysema can lead to cardiac insufficiency with much the same clinical picture.

Persistent diffuse abdominal pain with accompanying signs of peritonitis such as fever, vomiting, intestinal ileus, guarding, rebound tenderness and rigidity are usually indicative of a perforated hollow viscus. Confusing this clinical picture is the possibility that except for fever, these signs and symptoms might be present for several hours in a mild form without gastrointestinal perforation having occurred <sup>(58)</sup>.

Damage to the tympanic membrane, and middle and inner ear structures by blast is indicated by ear ache, tinnitus, some degree of hearing

loss, and occasionally vertigo. Unruptured tympanic membranes may demonstrate hemorrhagic blebs and be the cause of serosanguineous oozing from the external ear <sup>(10)</sup>. When only membrane rupture occurs, there is usually a temporary low tone loss on the order of 10 to 30 decibels and a high tone loss of 40 to 80 decibels until healing occurs <sup>(30)</sup>. Ossicular disruption produces a permanent conductive deafness for all frequencies. Full or partial recovery from acoustic trauma to the middle ear may be slow, often several months in duration <sup>(30)</sup>.

Possible late sequelae of blast include cardiac decompensation from extensive myocardial damage, recurrence of pulmonary hemorrhage, pneumonia, empyema and even lung abscess. They can become manifest and lead to "shock" and death up to several days after a blast exposure.

Recovery from blast injuries can be fast or slow, complete or incomplete. At best, especially if there have been neurologic manifestations, several days may be required for recovery, which may be surprisingly sudden and complete. Cardiac damage in blast tends to be permanent.

A careful medical assessment of an injured astronaut will be required as soon as possible after meteoroid penetration of a spacecraft cabin wall to determine not only the presence and severity of blast and other injuries mentioned in this chapter, but also to assess the immediate treatment needs of the astronaut. As a rule, the initial history and thorough physical will indicate the over-all injury severity. Close continuous observation will be necessary if there are any signs or symptoms of pulmonary, cardiovascular, nervous system or gastrointestinal involvement. Monitoring of the systemic arterial pressure and heart rate will bring to light any changes in cardiovascular status. If available on board a spacecraft, electroencephalography and electrocardiography might be used for establishing the presence of neurologic and cardiac involvement, respectively. X-rays could also be of some value in determining the degree of lung damage and the occurrence of visceral perforation.

Various measures which attenuate a blast overpressure or offer some

degree of body protection from the consequences of a blast wave can prevent or reduce the possibility of serious injury to an astronaut exposed to a meteoroid blast. The design of the spacecraft cabin structure so as to provide maximum attenuation of blast overpressures might be a highly effective measure. Although rigid thoracoabdominal shielding has been effective in reducing blast injury in animals, this measure might be too impractical for use in space <sup>(32, 62)</sup>. It should be pointed out, however, that lightweight thoracoabdominal shielding is also suggested for the protection of an astronaut from mechanical injuries while moving about in the spacecraft cabin (Chapter 14). Moreover, from discussion in Chapter 3, such shielding could also offer an astronaut a considerable reduction of risk of internally inflicted injuries from "explosive" decompression.

From the number and severity of different blast injuries and their sequelae, it is readily apparent that no outline of the definitive treatment of an astronaut who has been subjected to blast can be presented. Treatment must be based on sound clinical judgment, supported by a thorough understanding of possible blast effects.

Complete rest is considered to be absolutely essential for most blast injury cases <sup>(10, 27, 51, 58)</sup>. The work load on damaged lungs and heart must be minimized in order to reduce the risk of incurring further air embolization, pulmonary hemorrhage and edema, and cardiac decompensation. Sedation must be used with caution to prevent masking of various progressive signs which would indicate serious injury.

Positioning an astronaut in the head-down left lateral position in order to promote pulmonary drainage and minimize the migration of air emboli into his coronary and nervous system blood vessels, will obviously be of no therapeutic benefit in the weightless environment, but should be carried out under subgravity conditions. The early use of positive pressure breathing is contraindicated, for this measure may reopen alveolar-venous fistulae and introduce new showers of air emboli into the pulmonary veins <sup>(27)</sup>. Whole body pressurization to several atmospheres is a proven highly effective measure in the treatment of all air

embolic phenomena. For critical blast injuries, this measure would be required almost immediately after a blast, when most of the air embolization appears to occur (54, 58). The installation of a recompression facility on board the spacecraft for the treatment of air embolic phenomena is considered under the treatment of decompression sickness in Chapter 4. Since a space suit pressure of possibly up to 5 to 7 psia over the cabin atmospheric pressure might be attainable, a potential mechanism is available for increasing the total body pressure as well as for maximizing the partial pressure of oxygen administered to an astronaut when a recompression facility is not on board the spacecraft.

The administration of 100 percent oxygen might be indicated for the treatment of local (e.g., cerebral ischemia, myocardial ischemia) and systemic (e.g., pulmonary insufficiency, "shock") hypoxia. Since pulmonary hypoxia and reflexes caused by lung damage markedly constrict the pulmonary vessels, administering pure oxygen, which is a proven pulmonary vasodilator, might conceivably aggravate the tendency for lung hemorrhage and edema, and air embolization (2, 11, 19, 42, 54).

Whether increased oxygen tensions can actually overcome the protective vasoconstriction in a lung with blast injury is still open to question, however. Favoring the use of oxygen in the immediate post-blast period is the fact that any bubbles of pure oxygen in the cardiovascular system will be much more rapidly absorbed than bubbles containing an inert gas such as nitrogen (46). Hence the immediate administration of 100 percent oxygen - which probably will be part of the emergency decompression protocol following meteoroid penetration - should lower the risk of serious complications from air embolization. Because of the high mortality and serious sequelae of air embolization, oxygen should be used immediately after blast, in the hope that adequate reflex vasoconstriction and clotting will seal disrupted pulmonary vessels. Definitive studies on the effect of oxygen on vasoconstriction in a traumatized lung appear in order.

The question arises as to whether pure oxygen should be given beyond 30 minutes, which is considered the upper limit of the embolization period (54). Cyanosis or other signs of hypoxia would be a definite indication for continuing

or resuming oxygen administration. Because of the pulmonary vasodilatory effect of oxygen, the period of protective vasoconstriction might be prematurely shortened by this therapy. This failure of vasoconstriction has been shown in animal experiments to aggravate bleeding from vessels, disrupted by blast, especially if clotting is inadequate <sup>(8)</sup>. Again further experimentation is indicated.

The atelectatic tendency of pure oxygen must be kept in mind, especially in instances of treating severe lung injury cases with this gas <sup>(44)</sup>. As well, it should be noted that the prolonged administration of oxygen at a partial pressure above 400 mm Hg, as could be accomplished in a space suit within a pressurized spacecraft cabin could not only lead to primary pulmonary effects of oxygen toxicity such as toxic bronchitis and pneumonia with hyperemia and edema, but also markedly exaggerate the pathologic effects of blast on the lung <sup>(36, 45)</sup>.

Intravenous digitalization might be indicated for manifest cardiac decompensation <sup>(58)</sup>. A vasopressor, such as metaraminol, should be used primarily for the treatment of non-hemorrhagic "shock" <sup>(16)</sup>. Whether or not myocardial damage is suspected or evident, such a drug should probably be administered at the time of digitalization. Intravenous fluids should be used with extreme caution, especially during the first few hours after a blast exposure. A fluid overload could overstrain a damaged heart and aggravate pulmonary hemorrhage and edema. Therefore blood replacement agents, such as blood, plasma and dextran, used for the treatment of hypovolemic "shock" in space should be administered only if absolutely essential for the treatment of evident hemorrhagic "shock" from blast injuries.

The routine use of a vasopressor, even without evidence of non-hemorrhagic "shock", just to stop pulmonary bleeding is questioned. It is known that the bleeding following blast occurs from both the thin-walled subendothelial bronchial and pulmonary veins and capillaries <sup>(54)</sup>. Arteriolar and venous constriction should reduce this bleeding. Since vasopressors, such as levarterenol and metaraminol, constrict bronchial vessels to the same degree as peripheral vessels, and pulmonary vessels to a lesser degree, such a drug might be useful for decreasing



bronchial and possibly pulmonary hemorrhage (2, 3). However this indication for a vasopressor might be outweighed by the possibility that the damaged pulmonary vessels, which have been constricted by hypoxia and by local reflex action, might be opened by the increased pulmonary blood pressure and flow caused by the drug (2, 54). The beneficial effects of the vasopressor drugs primarily for the treatment of pulmonary complications of blast remain to be determined.

An analgesic, sedative or narcotic drug must be given with caution in the immediate post-blast period in order to prevent the possible masking of signs and symptoms which indicate serious injury. An antitussive, such as dehydrocodeinone bitartrate, might be indicated during the first few days after exposure to prevent hemorrhage due to excess coughing. A suitable broad-spectrum antibiotic will be required for peritonitis or pneumonia. It has been suggested that a suitable antibiotic-cortisone combination be administered as a prophylaxis for infection and to minimize pulmonary fibrous tissue formation for at least two weeks if severe lung damage has occurred (9).

Therapeutic pneumothorax as a "last-ditch" measure to control pulmonary hemorrhage, thoracentesis to remove air, fluid and blood from the pleural space, pericardiocentesis to remove pericardial fluid and blood, nasogastric intubation or gastrointestinal decompression for perforated viscus or temporary ileus, and laparotomy for perforated viscus are a few of the highly specialized procedures which may be necessary following a severe blast exposure (25, 31, 58, 60). These procedures would definitely require a specially trained astronaut and in many cases, a physician-astronaut. In the instance of a perforated viscus, facilities for performing abdominal surgery would also be necessary. Until such sophisticated treatment is possible in space, only more conservative supportive therapy will be available and a high morbidity and mortality from serious blast injuries in space must be accepted.

### Penetrating Injuries

Molten and fragmented meteoroid and wall materials ejected into the spacecraft cabin at high velocities could inflict a variety of single or

multiple penetrating injuries. Some associated burning of tissues is also likely. The majority of these missiles will probably be stopped by superficial tissues, with only small superficial lacerations being incurred. However, laceration of major vessels, nerves and other vital deep structures should still be considered possible. The treatment of penetrating injuries in space is discussed in Chapter 14.

One must also keep in mind the potentially great hazard of particles impinging on the eyes at the time of penetration and if these particles remain suspended in the weightless environment, for some time thereafter. Eye problems due to such foreign bodies are discussed in Chapter 8.

#### Meteoroid Penetration of the Space Suit

Little is known about the injuries which might result from meteoroid penetration of the space suit <sup>(4)</sup>. Fortunately it appears that through the use of a meteoroid bumper and absorbing materials in the outer layers of the suit, an astronaut will be reasonably well protected from such an event during extravehicular operations in space <sup>(6, 38)</sup>. What is presently thought to be an extremely low probability of penetration is apparent. If an approximate suit area of 25 square feet (2.5 square meters) and approximate thickness equivalent of 0.040 inch (0.12 cm) aluminum are applied to the "time to meteoroid perforation" data of Whipple (Figure 12.1), it is apparent that there is an extremely low probability of penetration, even though there is a level of uncertainty of about one order of magnitude surrounding this estimate <sup>(4)</sup>. It is noted that the degree of protection offered by the "shatterproof" space suit helmet and visor materials is many times greater than that offered by other parts of the suit <sup>(4)</sup>.

Molten and vaporized meteoroid and suit materials, and fragmented meteoroid might come into close contact with or impinge on the skin of an astronaut if a space suit is penetrated. An "explosive oxidation" of vaporized materials will probably also occur at the site of penetration. Experiments which are attempting to simulate meteoroid penetration of the space suit in space are demonstrating that the suit materials do not

tear from or spall at the site of penetration and that these materials are not ignited by the penetration even at maximum suit pressurization with 100 percent oxygen (6, 38). From these studies, it appears that the most likely injury an astronaut will sustain during a penetration of the space suit by a minimum penetrating meteoroid will be a circular-shaped burn at the site of penetration. This burn area might vary from several millimeters to a few centimeters in diameter, depending on the magnitude of the penetration. Undoubtedly the degree of tissue damage by burn will be greatest in the central part of this area. The management of burns in space is discussed in Chapter 13.

Single or multiple meteoroid fragments of larger penetrations might also penetrate the skin and subcutaneous tissues to a variable depth. Due to their high temperatures, these fragments might also produce some thermal damage of the tissues. The majority of these missiles will probably be stopped by superficial tissues with only small, superficial lacerations resulting. However, laceration of major vessels, nerves and other vital deep structures should still be considered possible. The management of such penetrating injuries is discussed in Chapter 14. Finally, if the size of the hole produced by a penetration is so large that the pressure in the space suit cannot be maintained long enough for an astronaut to carry out emergency measures such as returning to the spacecraft, he might be subjected to the decompression effects (Chapters 1, 2, and 3).

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## CHAPTER 13

### BURNS

In this chapter, the characteristics and principles of management in space of thermal, electrical, and chemical burns will be briefly discussed. It must be kept in mind that a relatively minor burn of a functionally important body area such as a finger or eye could seriously reduce the operational capabilities of an astronaut for a prolonged period of time. Moreover, intensive supportive therapy and definitive surgery normally employed in the treatment of major burns will probably not be possible in space in the foreseeable future. The importance of ensuring maximum burn protection as well as the best therapy possible for burns during space operations cannot be overemphasized.

It should also be mentioned that if programmed decompression-recompression of a spacecraft cabin is ever to be employed for extinguishing a fire or removal of toxic products of combustion or chemical contaminants from a cabin atmosphere, a protected astronaut could suffer acute hypoxia (Chapter 1), and possibly ebullism (Chapter 2) for a short period of time. Although a much less effective immediate emergency measure, purging of the atmosphere with an inert gas such as nitrogen could also lead to acute hypoxia.

#### Thermal Burns

Design of spacecraft cabins to provide optimum fireproofing and protection from meteoroid penetration, and the installation of adequate fire detection and extinguishing systems should reduce the risk of thermal burns in space to a minimum. The influence of various possible space atmospheres on this risk has been intensively assessed by Roth (45, 46).

It is readily apparent that the type and degree of a thermal burn suffered by an astronaut in space will be determined by one or more of many factors. The relation of time and intensity of applied thermal

energy to burn severity has been discussed in detail by many authors (6, 14, 19, 34, 36, 40, 41) and will, therefore, not be considered here.

From a causative standpoint, if a meteoroid should penetrate a spacecraft cabin wall (Chapter 12), a localized, possibly deep burn anywhere on the body could be produced by contact with the flash or by being struck with molten and hot fragments of both meteoroid and wall. Such a burn could also follow meteoroid penetration of a space suit.

A serious linear thermal burn, most likely of the hands, could result from contact with a wire rendered hot by short circuit. A fire in a spacecraft cabin could burn large areas of an astronaut's body. Assuming that fire resistant clothing is worn, only exposed skin areas, such as his face, neck, arms and hands might be burned. Although space suit materials will have a high melting point, heat transfer from fire in contact with the suit might be sufficient to cause extensive thermal skin injury. Respiratory tract damage from the inhalation of hot air and gases of combustion is considered a major potential consequence of unprotected exposure to a fire in a "closed" space environment.

### Characteristics

Burns of the skin can be divided into three categories - first, second, and third degree burns. First and second degree burns are referred to collectively as partial-thickness burns. Third degree burns are also termed full-thickness burns.

A first degree burn is similar to the familiar "sunburn". It involves only the superficial or outer layer of the epidermis. Erythema, pain, and occasionally slight edema of the involved skin subside within one or two days. During this time, the area is dry, warm, and tender. Destruction of the superficial epidermis to a sufficient depth can lead to scaling, often with an associated severe itching sensation, during the healing phase. Infection of this damaged skin does not characteristically occur.

A second degree burn is slightly deeper than a first degree burn. It involves all the layers of the epidermis. Small islands of germinal cells which remain in the deeper corium eventually reform an intact

epidermis. Blisters, severe pain, and marked subcutaneous edema are characteristic. Removal of blistered tissue leaves a pink, moist, extremely tender surface. Healing occurs uneventfully in 14 to 21 days unless infection supervenes <sup>(4)</sup>. A deeper second degree burn can be readily converted into a full thickness burn by infection.

In a third degree burn, the entire dermis and corium down to the subcutaneous fat are destroyed. Deeper tissues such as large blood vessels, nerves, muscle and tendon may also be involved. The destroyed skin is insensitive, white or charred in appearance, and dry. Subcutaneous edema is usually more marked than in the second degree burn. In the neck, this edema can produce airway obstruction. In an extremity, it can seriously jeopardize blood flow to the whole or distal part of the extremity. The dead tissue, or eschar usually begins to separate from the living tissue within two to three weeks, and eventually leaves an open wound. If this wound is too large to be covered by normal skin and if it is not covered with a skin graft, a thick layer of granulation tissue can form. Over a period of many months, this tissue becomes a scar and can produce severe contractures of the burn area. It should be remembered that burned dead tissue provides an excellent medium for bacterial growth, so that third degree burns tend to become infected.

Inhalation of hot air, and irritant smoke and gases produced by a fire can lead to some degree of injury to respiratory tract tissues <sup>(15, 20, 31, 42, 43, 44, 47)</sup>. Even though involvement below the larynx is usually prevented by reflex glottic closure, lower respiratory tract damage is considered to be more likely to occur in a spacecraft because of the rapid spread, high concentrations, and persistence of the products of combustion in a confined environment <sup>(31)</sup>. An edema of rapid onset in the larynx and epiglottis might seriously obstruct air flow <sup>(4)</sup>. Involvement of the lungs is usually extensive and bilateral <sup>(42)</sup>. With extensive alveolar damage, survival is highly improbable <sup>(39)</sup>. The damaged tracheobronchial mucosa and alveoli can immediately become edematous and can produce sufficient transudate to cause death from suffocation <sup>(31)</sup>. A severe irritative bronchospasm may also

be a factor in producing asphyxia <sup>(15)</sup>. Infection of a damaged respiratory tract usually becomes evident within three days <sup>(42)</sup>. An exudative tracheobronchiolitis usually leads to massive or patchy atelectasis, bronchopneumonia, and all too frequently, death <sup>(42, 47)</sup>. Respiratory tract damage should be suspected if there is a facial burn, singeing of the nasal hair, redness of the pharyngeal mucosa, hoarseness or rales in the chest <sup>(39, 43)</sup>. Serious damage is indicated by severe substernal pain, coughing of abundant fluid, and cyanosis.

Burn deaths result from a number of causes other than respiratory tract damage. In extensive second and third degree burns, a rapid excessive loss of protein-rich intravascular fluid into the involved skin to form blisters and into the involved subcutaneous tissues to form edema, may result in profound "shock" unless this fluid is adequately replaced. As discussed in Chapter 10, it is not known to what degree the tendency for "shock" to occur from loss of fluid from the circulation will be aggravated by the decrease of fluid volume which appears to result from exposure to weightlessness. For an unknown reason, paralytic ileus often occurs after an extensive burn and can, especially if oral fluids are administered, lead to vomiting <sup>(4)</sup>. Fatal aspiration, a not uncommon event in a moribund burn patient, would be even more likely to occur in the weightless space environment (Chapter 8). The vomitus could also be a serious particle and droplet hazard to other astronauts. Beyond the first few days after a burn, death can occur from an overwhelming septicemia, in most cases by hemolytic Staphylococcus aureus or Pseudomonas aeruginosa <sup>(2)</sup>. These highly pathogenic organisms usually enter the blood stream from a suppurating burn wound. Also during this period, death occasionally occurs due to hemorrhage from an acute upper gastrointestinal, or so-called Curling's ulcer <sup>(4)</sup>.

Weight loss, accompanied by marked negative nitrogen balance, characteristically occurs in an extensively burned individual. It is proportional to the extent of the burn, and is restored at a rate which depends upon the adequacy of the nutritional regimen, the time of removal of necrotic tissue and closure of the burn wound, and whether

or not wound infection is present. It has recently been noted that a significant amount of this weight loss can be attributed to an excessive metabolic demand placed on the body secondary to heat loss from fluid vaporization from the burn surface <sup>(38)</sup>. Various measures to restore the water barrier to burn areas have apparently successfully reduced this strain on the body <sup>(28, 37, 38)</sup>.

Mild to severe anemia can appear in the period immediately following, or several days after a burn. Deep burns can immediately destroy or increase the fragility of exposed red blood cells. Anemias which appear later are attributed mainly to a combination of suppressed red cell production due to inadequate nutrition, toxins from necrotic tissue and bacteria, and red cell loss from the wound site.

### Diagnosis

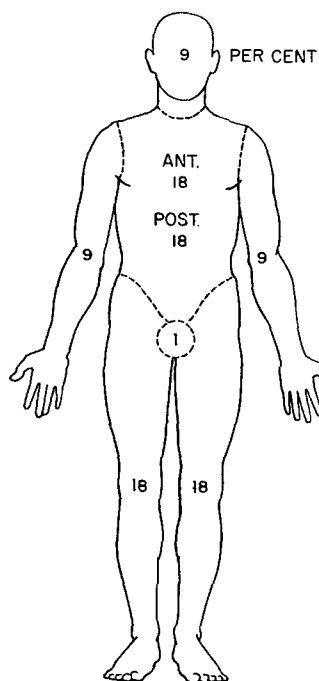
Initially, it can be difficult to distinguish a second from a third degree burn. The diagnostic characteristics of the three degrees of burns have been pointed out above.

A reasonably accurate estimate of the total burned surface area is important, especially to determine whether fluid therapy is needed, and if so, the amount of fluids which should be administered. A rapid popular method is the "Rule of Nines" shown diagrammatically in Figure 13.1 <sup>(4, 5)</sup>. It is not as accurate, however, as the Lund and Browder chart, pictured in Figure 13.2 <sup>(4)</sup>. Best use can be made of such a method after the burn wound has been cleansed and all loose, devitalized tissue removed. For estimating fluid requirements, the total burn area estimated by either of these methods is the sum of the second and third degree areas only.

If ever possible in space, various laboratory procedures can be of benefit in the assessment and therapy of a seriously burned astronaut. These procedures and the rationale of their use are discussed below.

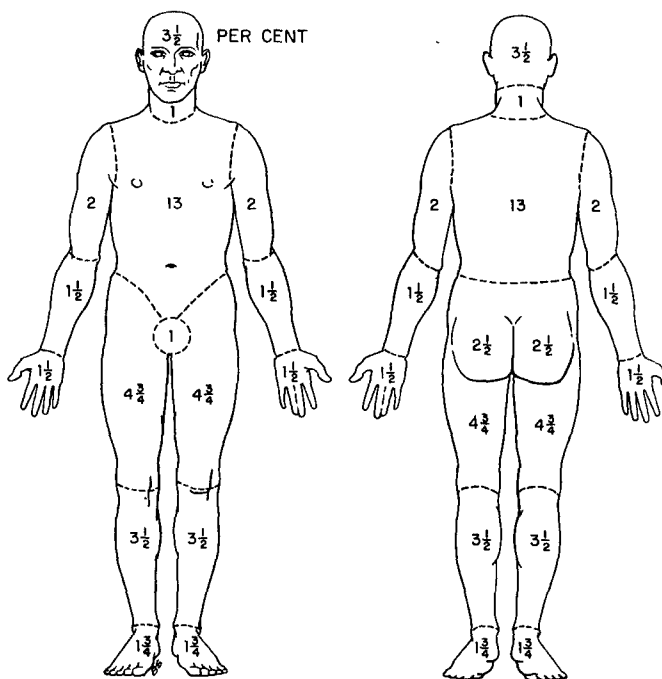
### Treatment

Minor burns - Partial-thickness burns covering less than 10 percent of the body surface area, or full-thickness burns of less than



Total Per Cent Burned  $\underline{\hspace{1cm}} 2^\circ + \underline{\hspace{1cm}} 3^\circ = \underline{\hspace{1cm}}$

Figure 13.1 The "Rule of Nines" (Adult)



Total Per Cent Burned  $\underline{\hspace{1cm}} 2^\circ + \underline{\hspace{1cm}} 3^\circ = \underline{\hspace{1cm}}$

Figure 13.2 Lund and Browder Chart (Adult)  
(After American College of Surgeons <sup>(3)</sup>).

2 percent are considered minor burns <sup>(4)</sup>. Milder first degree burns may involve a much larger area. Fluid replacement for minor burns is usually not required.

First degree burns require no special care. The surface should be protected from irritating garments. A topical anaesthetic, such as 1 percent cinchocaine ointment, may provide some relief of pain and tenderness.

It is recommended that all second and third degree burns, except possibly of certain areas of the face, be treated in space by the so-called "closed" method. This measure will provide less risk of wound infection and further trauma of burned tissue, provide greater comfort, and prevent the release of infected wound material into the spacecraft cabin environment. First, any loose dead tissue, except blisters on the palm of a hand or sole of a foot, should be debrided and if required, the involved surface gently washed with isotonic saline solution. Then the burned surface should be covered with an evenly placed layer of either fine-mesh gauze, petrolatum gauze, carbowax gauze, or a commercial nylon preparation. Finally, a layered, occlusive burn dressing should be applied.

Although locally applied anti-bacterial agents have in general not been successful in preventing and controlling burn sepsis in the past, success has recently been reported with 0.5 percent silver nitrate solution and with 10 percent mafenide acetate cream <sup>(5, 24, 28, 33, 37)</sup>. For reasons which are readily apparent in the writings cited and because it could present a serious droplet hazard in space, silver nitrate solution does not appear suitable for use in space. On the other hand, if mafenide acetate cream is found suitable for use in space, it might be impregnated in the initial layer of a burn dressing. This water-rich cream has controlled burn wound sepsis, involving even Pseudomonas aeruginosa. It has also minimized weight loss from vaporizational heat loss, from toxic products of bacteria and tissue breakdown, and from inadequate dietary intake associated with repeated general anesthesia for extensive wound debridement. Further clinical use of mafenide



acetate is required before it can be recommended for burn treatment in space.

A burn should be redressed at least every 5 to 7 days. Infected wounds often require more frequent dressing changes. Adherent dressings should be moistened with saline, particularly if over second degree burns, in order to prevent damage to delicate newly formed epithelium. Although some necrotic and liquified burn tissue will be removed along with the dressing, any remaining in the wound should be debrided surgically, especially if the wound becomes infected. Enzymatic debridement of necrotic burn tissue has not proven to be of practical value (4, 8, 26). It is important to note that extreme care must be taken to prevent the release of infected material into the spacecraft cabin atmosphere. This might be accomplished by means of various suction techniques. A suitable mask should be worn by anyone potentially exposed, including the injured astronaut. An analgesic drug should be administered with care during the immediate post-burn period. It can be used thereafter as required, especially at times of dressing change and surgical debridement.

On the whole, systemic antibiotic therapy has been relatively ineffective in controlling burn wound infections. This generally fails to provide bactericidal levels of drug in infected avascular burn tissue, and promotes the emergence of antibiotic-resistant organisms and sensitizes patients to anti-bacterial drugs (26, 33). Tetanus anti-toxin or toxoid will probably not be required in space if astronauts have been immunized against tetanus prior to space missions.

Major burns - All partial-thickness burns affecting more than 25 percent of the body surface area, or full-thickness burns of more than 15 percent may be considered as major burns (5). These burns fall into the "potentially lethal" category. They usually require intensive therapy. This therapy centers mainly on providing adequate fluid replacement for the protein-rich fluid lost in burn blisters and edema, minimizing vaporizational fluid losses from the burn surface, protecting the burn from and treating secondary infection, undertaking as much debridement of burn tissue as possible whenever feasible,

closing full-thickness wounds as soon as possible, and maintaining the nutritional status of the patient. It can be expected that if intensive therapy, in particular definitive surgery such as extensive wound debridement and skin grafting cannot be undertaken in space, the usually severe morbidity and high mortality associated with major burns will be markedly increased. This will, of course, be the case for many years to come. Hence a regimen similar to a "shelter plan" may only be possible. A completely austere approach would include medication for pain, proper positioning of affected parts, oral fluids, wound coverage which might be of the simplest sort (e.g. plastic bags for hands), and the use of an oral airway in instances of facial edema and respiratory tract damage <sup>(7)</sup>. Even if intravenous fluids are carried on board a spacecraft, their use might not be feasible for severe extensive burn lesions.

Burn depth and extent should be assessed as soon as possible according to the criteria discussed above. Second and third degree burn areas are added for determining fluid requirements. Intravenous fluids are usually administered as soon as possible to individuals who have more than 25 percent burns <sup>(5)</sup>. They may also be given for burns of lesser extent but of greater depth, or for burns with marked edema. As noted in Chapter 10, it is considered possible that due to a decrease of circulating blood volume in the weightless space environment, the tendency for "shock" to occur from intravascular fluid loss in burns might be greater in space than on Earth. Accordingly, appropriate changes might have to be made in any Earth-based formula to be used for estimating fluid replacement for major burns in space.

One of the most popular formulae used to estimate the amount of fluid required by a burned individual is the so-called "Brooke Formula". It states that each of the following fluids should be given intravenously in the first 24 hours after a major burn is sustained <sup>(4)</sup>.

COLLOID (0.5% dextran, plasma or blood)

0.5 ml/Kg/% of body surface burned.

ELECTROLYTE SOLUTION (Ringer's lactate or isotonic saline)

1.5 ml/Kg/% of body surface burned.

WATER REQUIREMENTS (5% glucose in water)  
2000 ml.

One-half of the fluids required in the first 24 hours should be administered over the first 8 hours, and one-half over the remaining 16 hours. In the second 24 hours, about one-half of the first 24 hour requirement is recommended. Burns of more than 50 percent of the body surface are calculated as for 50 percent burns, or an excess quantity of fluid can be administered. It is noted that these fluids should be administered with great care if the respiratory tract has been damaged, in order to prevent the initiation or aggravation of pulmonary edema.

Dextran has been considered as effective as plasma in fluid replacement for burns (4, 9, 26). Opinion to the contrary may have been due to the fact that larger molecular weight dextran preparations used in the past may cause some interference in clotting time and may promote agglutination of red blood cells (26). The use of blood, even if carried on board spacecraft, in early burn therapy is quite controversial. It is currently thought that blood should be reserved for individuals who have a proven decrease in circulating red cell volume (33). Ringer's lactate solution is preferable to isotonic saline because a burned individual tends to develop metabolic acidosis in the early post-burn period (4). In fact, Moyer and coworkers (38) have advocated the use of only Ringer's lactate solution, with its pH adjusted to 8.2, for the treatment of burn "shock". Their reported success with this agent indicated to them that burn "shock" is not primarily oligemic in origin, but is mainly due to an extravascular sodium deficiency resulting from the thermally injured, vascularly isolated tissues taking up large quantities of salt and water. They suggested that Ringer's lactate solution be given fast enough during the 24 to 36 post-burn hours to keep the burned individual safely alive, making urine and remaining oriented - but not so fast or in such quantity to raise central venous pressure significantly and sustainedly above normal. As to whether Ringer's lactate solution will become the sole recommended infusate for burn "shock" will depend upon the results of further clinical use of

this agent.

The great quantities of intravenous fluids are administered to burned individuals through one or more large bore (18 gauge or larger) needles or polyethylene cannulas inserted into a large vein through the skin or by cut-down. At the time of an initial venipuncture, blood can be taken for hematocrit. A narcotic agent, such as morphine, may be administered intravenously, but only if absolutely required for apprehension and pain (4, 5).

The best single indication of the adequacy of fluid therapy is probably an hourly urine output between 20 and 50 ml. This should be determined continuously by means of an indwelling urinary catheter, especially if large areas of the body surface are burned. The catheter can usually be removed within 2 to 3 days. While it is in place and at least for a week after its removal, a suitable urinary antibacterial agent, such as sulfadimethoxine, should be administered.

Venous pressure is an excellent parameter that can be used to avoid over-transfusion. It is generally agreed that to obtain a valid measure of venous pressure, it is necessary to introduce a catheter into the vena cava or right atrium. There appears to be no reason, however, why measurements of venous pressure made in a large peripheral vein should not be valid in the weightless environment.

In a situation where the exact state of total body hydration is in doubt, the serum sodium concentration, if ever possible to determine in space, would be an especially useful guide to fluid therapy. A decrease in serum sodium indicates an excess of body water, and an increase, an excessive water loss. The latter, which is often seen in burn patients who have an enormous insensible water loss, indicates the need for water without salt, rather than more dextran or plasma. (11).

The value of the hematocrit in assessing the adequacy of fluid therapy in burns is presently being debated, since the pathophysiology of the changing red cell mass in a burn is complex and hemoconcentration is a result of more than the loss of plasma (11, 38). Therefore the efficacy of the hematocrit must be thoroughly assessed before recommending its use in space.

Several other points should be kept in mind when determining the adequacy of fluid therapy in burns. A fluid deficiency can be indicated by severe thirst, tachycardia and systemic arterial hypotension. On the other hand, it is important to point out that blood pressure and pulse can be maintained at normal levels at the expense of a drastic vasoconstrictive reduction of the peripheral vascular bed. Interestingly, death from burn "shock" is often slow, whereas death from hemorrhagic "shock" is often sudden <sup>(38)</sup>. It should be noted that restlessness, irritability, and disorientation are manifestations of a fluid deficit, the treatment of which is fluid, not a narcotic. Abnormal venous distension and the appearance of rales in apparently undamaged lungs point to a fluid excess.

If the urinary output remains low in spite of an apparently adequate restoration of blood volume and tonicity, some degree of renal failure might have resulted from a period of "shock". Further intravenous fluids should then be given with extreme caution, especially if the lower respiratory tract might be damaged. As pointed out in Chapter 14, the usefulness of an intravenously administered osmotic diuretic, such as mannitol, for preventing renal failure from "shock" has been well established. Whether this agent can also be employed to prevent or reduce burn edema should be investigated, for it is considered possible that edema can contribute markedly to the amount of tissue devitalization resulting from a burn <sup>(47)</sup>.

Since a paralytic ileus, often with accompanying vomiting, frequently occurs in severe burn cases, an astronaut suffering from a major burn should not have any oral intake until it is assured that he is passing gas per rectum, his abdomen is not distended, and good bowel sounds are heard on auscultation <sup>(25)</sup>. Particular care must be taken when oral fluids are eventually administered, since vomiting in the weightless environment will create a serious droplet hazard (Chapter 8). In fact, if there is a possibility of vomiting in the post-burn period, nasogastric intubation should be performed.

Although a burn patient might be able to tolerate his metabolic food requirement and large amounts of fluid taken orally, large quantities

of intravenous fluid might still be required after 48 hours because of a marked diuresis due to the reabsorption of edema fluid. Since the body tends to retain sodium at this time, the replacement fluid should be 5 percent glucose in water. Serum sodium determinations would be valuable for assessing the state of sodium balance. Potassium (40 to 80 mEq/day) should be given intravenously if this form of therapy is continued beyond 3 days and there has been an inadequate oral food intake.

A tracheostomy might be indicated if serious respiratory tract damage occurs or if there has been a deep burn of the face and neck. The risk of infection spreading from a septic burn wound and involving the tracheostomy and lower respiratory tract should be kept in mind when assessing the need for this measure, however. Although one would prefer to wait as long as possible before performing a tracheostomy in the space situation, it must be remembered that laryngeal edema can occur quite rapidly and this procedure will be difficult after edema forms in a burned neck.

The prophylactic use of antibiotics in the treatment of major burns is presently being debated <sup>(47)</sup>. Systemic antibiotics of whatever combination are of value only in the first six to seven days, during which they can prevent septicemia <sup>(47)</sup>. These drugs should be added to the intravenous fluids in order to maintain continuous high levels in blood and tissues, especially during the first two to three days after a burn. Thereafter the intramuscular route of antibiotic administration is considered adequate. Burn wound or respiratory infection attended by a high fever will usually indicate the need for an increase in dosage, the addition of a different antibiotic or a change to an entirely different antibiotic regimen. Antibiotics might be selected on the basis of culture and sensitivity studies of bacteria taken from the wound, if such studies are ever possible in space. Otherwise, a rather "shotgun" therapeutic approach will have to be used. The possible usefulness of locally applied mafenide acetate cream for the prevention and control of burn wound infection in space has been discussed above. The early removal of dead tissue in preventing the ravages of the septic or autolytic phase

of burns cannot be overemphasized.

The local treatment in space of major burns will be the same as that discussed above for minor second and third degree burns. It must be remembered that eventual closure of third degree burns by skin grafting will have to be undertaken after completion of the mission, so that up to this time the treatment of these burns will be aimed at providing the best supportive therapy and wound care possible in space. However, in the very prolonged mission where extensive skin grafting is not possible, strips of skin taken under local anesthesia by means of an air-driven dermatome might be very advantageous <sup>(5)</sup>.

Respiratory tract damage - A definitive treatment regimen for respiratory tract damage by hot air, and smoke and gases of combustion has not been established <sup>(7)</sup>. It is possible that intensive therapy with steroids, as in the treatment of chemical inflammation of the lower respiratory tract (Chapter 8), might be of considerable value, not only to combat acute inflammatory edema and bronchospasm but also to reduce tissue necrosis which can eventually lead to infection, bronchiectasis and bronchial stenosis <sup>(15)</sup>. It is suggested that a suitable steroid, such as dexamethazone, be inhaled in its nebulized form and be administered systemically. Bronchospasm might also be combatted with nebulized isoproterenol or intravenous aminophylline <sup>(15)</sup>.

Otherwise, the treatment of this type of respiratory tract damage is supportive. A tracheostomy appears to be of little value except to relieve early acute localizing obstruction <sup>(31)</sup>. It might also be required for suction of copious quantities of exudate from a seriously involved lower respiratory tract. Oxygen administered under positive pressure might successfully combat pulmonary edema and hypoxia <sup>(7)</sup>. Intensive broad spectrum antibiotic therapy is indicated in all cases with respiratory tract damage.

Burns of the hand - The astronaut's hands are thought to be one of the most likely parts of his body to suffer thermal injury in space.

For this reason, and since serious functional impairment can follow even a relatively minor burn of a hand, the treatment of these burns deserves special mention here.

Burn blisters on the palm of the hand have a thick covering which should not be broken or removed at the time of their initial dressing. The occlusive dressing should be applied lightly in such a way as to immobilize the hand and fingers in a position of function. Care must be taken to place the dressing between the fingers. A splint may be or may not be used. Again, debridement should be as thorough as possible at the time of each dressing change. The requirement for early vigorous physiotherapy of a burned hand cannot be overemphasized (32).

Recently, a fabricated mitten type of dressing, saturated with silicone fluid and covered with a plastic bag, has been utilized in the treatment of burned hands (29). This dressing is changed daily. Finger motion is maintained and removal of eschar and exudate is apparently considerably enhanced. This technique has also reduced the need for skin grafting and has decreased both the extensive care usually required and the morbidity associated with this injury. It is thought that this approach to the treatment of hand burns and possibly cold injuries (Chapter 7) might be especially suited to the space situation, particularly for the reason that some degree of hand function can be maintained.

#### Electrical Burns

Even though spacecraft electrical systems should be adequately shielded, astronauts might be exposed to an electrical burn hazard if a system is disrupted by a docking or landing accident, or by meteoroid penetration, or if they must make repairs on a system in space. Electrical burns characteristically penetrate deeply into tissues, so that even a small electrical burn of the hand, which is considered by far to be the most likely site of this injury, could produce



marked functional impairment of an astronaut.

### Characteristics

For an electrical injury to occur, some part of the body must be interposed between two conductors having different electrical potentials. The current which flows between the conductors tends to follow the most direct path possible. Its type (alternating or direct), intensity, path and duration of flow are the major determinants of the pathophysiologic disturbances it produces. These determinants have been discussed extensively in the literature (12, 13, 17, 21, 22, 23, 35).

Most important to note is the fact that an alternating current is more harmful than a direct current, especially in the 60 cycle range which is particularly disturbing to cardiac and respiratory function (35).

The most frequently observed pathophysiologic disturbances from current flow through the body have been cutaneous burning, deep burning with progressive necrosis, fracture of bones or dislocation of joints by violent uncoordinated muscular contractions, and immediate death from circulatory or respiratory arrest (10).

The degree and site of an electrical burn is determined by the resistance which a tissue offers to current flow (35). Because dry skin has a high electrical resistance, electrothermal injuries are usually limited to it and immediately subjacent tissues. On the other hand, moist skin has a much lower resistance than dry skin, so that deep burning, especially of muscle, can result from electrical contact.

If the contact between the skin and an external conductor is large, the generation of heat per unit area of surface may be inadequate to produce a burn, yet the current flow may be more than enough to paralyze respiration or produce ventricular fibrillation (35). Conversely, the heat generated at the site of a small contact, may be sufficient to produce a severe burn, even though the current flow through the body is inadequate to cause a significant degree of physiologic disturbance.

Electrical burns are in most cases deeper than ordinary flame burns (4). Some degree of coagulation necrosis occurs in the skin and

deeper tissues. A major feature is the extensive vascular thrombosis which usually occurs in surrounding tissues over a period of hours to several days after an electrical burn is inflicted. Consequently, the extent of injury usually does not become apparent for up to several days, and is always much more severe than originally anticipated (4, 16). Deep structures which are often involved include muscle, blood vessels, nerves, tendons, and even bone. In the hand, all of these structures are in close proximity to one another and to the surface, so that electrical burns of the hand tend to be extremely serious. Because of both the tendency to grasp a wire and the spastic grip produced by electric current flow up the arm, burns on the palm of the hand occur much more frequently than on its dorsum.

Extensive muscular damage can lead to a variety of serious secondary consequences. Loss of potassium from damaged muscle can produce a hyperpotassemia sufficient to give rise to severe failure of cardiac function (17). Hyponatremia can result from a large scale afflux of sodium ions into severely affected muscle. Release of myoglobin and hemoglobin from hemolysed red cells can lead to anuria and fatal uremia. Damaged muscle is particularly prone to become infected (4).

An electrical burn is usually white or charred, and insensitive. Local edema can be quite marked and, when combined with the tissue necrosis, can give the wound the appearance typical of moist gangrene (4).

One of the most serious complications of electrical burns is hemorrhage, resulting from necrosis often of the walls of major vessels (4, 16). Profuse arterial or venous bleeding might occur.

### Treatment

In general, an electrical burn is managed in a similar fashion to a thermal burn. More intensive fluid therapy is usually required in electrical injuries than in thermal burns (5). The administration of potassium should, of course, be restricted.

One must be sure that there is no muscle damage beneath a full-thickness burn eschar (5). When dead muscle is present, it must be

excised. However, an extensive wound debridement may be difficult if not impossible to undertake in space in the foreseeable future.

Since acute renal failure occurs not uncommonly following large electrical burns, an osmotic diuretic, such as mannitol, might be given if the urinary output is low, in spite of adequate fluid administration <sup>(4)</sup>. Alkalinization of the urine with intravenous and oral bicarbonate might reduce the damaging effects of myoglobin and hemoglobin on the kidneys <sup>(17)</sup>.

If there is no dead muscle, it is recommended that an electrical burn not be debrided until ten to fourteen days, when the living and dead tissues are well demarcated <sup>(5)</sup>. Since hemorrhage is a common complication of electrical burns, great care must be taken with debridement close to major blood vessels. It is difficult to stop bleeding by local pressure or even hemostatic agents, such as gelfoam or topical thrombin. Arterial bleeding might have to be arrested by ligature.

Finally, if circulation or respiration are arrested by an electrical shock, resuscitative measures discussed in Chapter 1 may be undertaken. It is thought that permanent respiratory arrest is unlikely unless an electrical current is sufficiently great to cause gross burning <sup>(23)</sup>. Hence artificial respiration might have to be carried out for a prolonged period of time before adequate breathing returns.

### Chemical Burns

The burn hazard presented by a corrosive chemical spilled by accident into the spacecraft cabin atmosphere will be greatly magnified in space, for not only will droplets and particles tend to remain suspended in the weightless environment, but also their atmospheric dilution will be limited by the confined environment of the spacecraft cabin. Such a hazard must be seriously considered when analytical systems requiring replacement chemicals are carried on board spacecraft. Notably, a caustic burn hazard will exist while servicing life support systems which contain lithium hydroxide or a superoxide as the

carbon dioxide absorbent.

### Characteristics

Corrosive chemicals include mineral acids and alkalis, strong organic acids and alkalis, and inorganic oxidizing agents. Many also possess systemic toxicity, even if absorbed only through the skin. All these agents are protoplasmic poisons through their ability to produce protein hydrolysis, either by a hydrogen or hydroxyl ion effect.

Acute chemical injury of the skin is in many ways similar to that produced by heat <sup>(4)</sup>. In fact, injurious effects of chemicals are sometimes due in part to the development of heat. A highly variable picture of injury may be present. Of interest is the fact that alkalis tend to penetrate and so burn deeply into tissues, whereas acids burn more superficially. Severe burns are characterized by a central zone of necrosis, surrounded by less damaged, more hyperemic, partial-thickness burn areas. Chemical injuries of the eyes and respiratory tract are discussed in Chapter 8.

### Treatment

Immediate irrigation of the involved area of the body with copious amounts of water still remains the best emergency measure for chemical skin burns. Not only does water carry away the chemical, but also the heat of dissolution. This might be accomplished in space with a special body cleansing apparatus. Another suitable measure might be the immediate application of materials soaked with water or a suitable neutralizing or buffering agent to the area of contact. Any irrigation procedure should be carried out for at least 10 minutes or even longer, especially for alkali burns. Other than such an emergency procedure, the treatment of chemical burns will be similar to that described previously for thermal burns.

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## CHAPTER 14

### INJURIES FROM MECHANICAL FORCES

Astronauts will face a potential risk of injuries from mechanical forces during operations in space. Many causes of this form of trauma can be envisaged. While some injuries may prove to be peculiar to the space environment itself, any type and severity of mechanical injury is possible.

This chapter briefly discusses possible causes, prevention, and principles of diagnosis and treatment of mechanical injuries during missions in space. Notably, it above all others raises the question as to what level of medical care might be given in space. It would seem reasonable that one or more astronauts should be trained in the essential requirements of handling medical problems which might occur in space. However, as is apparent throughout this report, the clinical judgment and skills of a physician-astronaut would be highly desirable for the optimum handling of such problems. The topic will be discussed in greater depth in Chapter 16.

The possibility that the healing of various wounds might be altered to some degree by the weightless environment or by spacecraft atmospheres should be kept in mind. This is an area to which no significant research contributions appear to have been made.

#### Causes

While moving freely about in the weightless environment of his spacecraft cabin, an astronaut might misjudge the velocity and direction of motion which he imparts to his body <sup>(7, 10)</sup>. As a result, he might sustain an injury by striking an immovable structure, especially a protruding sharp edge or corner. It is also possible that if unrestrained, he might be injured by being thrown about in the cabin or by being struck by displaced objects during maneuvering, docking, and landing operations. There might be some risk of mechanical injury associated with servicing and repair procedures within the spacecraft. Most injuries in the above situations will probably be of a minor nature, such as abrasions, lacerations, and

contusions. On the other hand, high momentum accidents might lead to more serious consequences, such as concussion and fractures.

As was pointed out in Chapter 12, a great variety of minor and major mechanical injuries could result if a meteoroid should penetrate the wall of the spacecraft cabin. Molten and fragmented meteoroid and wall materials ejected into the cabin at high velocities could inflict single or multiple penetrating injuries and lacerations, probably with some associated burning of tissues. Particles could enter the eyes and produce a variety of problems discussed in Chapter 8. Such injuries might also be produced in partial penetration conditions by metal fragments which spall from the inner surface of the cabin wall. It is conceivable that a translational wind load from a meteoroid blast could be of a sufficient magnitude to create missiles of disrupted cabin structures or force an astronaut against immovable structures in the cabin. If this event should occur, any number of mechanical injuries similar to those discussed below for "explosive" decompression might result.

As discussed in Chapter 3, mechanical injuries might be inflicted externally during an "explosive" decompression of the spacecraft cabin, especially if an astronaut is unrestrained and is either close to the decompression orifice or in a narrow passageway between parts of the cabin. As well, items of equipment or other materials in the cabin might detach or fragment at the moment of decompression and become missiles. This hazard will probably be greatest if the cause of the decompression is a meteoroid penetration. Closed wounds such as contusions and fractures might result if an astronaut is thrown against immovable structures by the blast of escaping air. Violent blows to his body might disrupt hollow viscera and produce contusions or lacerations of solid organs, particularly in the abdominal region. Chest trauma might result in single or multiple rib fractures, hemothorax, pneumothorax, and pulmonary or cardiac contusion. Possible craniocerebral injuries include skull fracture, concussion, cerebral contusion or laceration, subdural or extradural hematomas, chronic subdural hematoma and damage to the labyrinthine system. Open wounds such as abrasions, lacerations and penetrating injuries might result not only if an astronaut is flung against sharp protruding

structures in the spacecraft cabin, but also if he is struck by various missiles. These wounds may involve superficial tissues or vascular, nervous, skeletal or visceral structures, leading to death of an astronaut.

An astronaut might also be injured during an extravehicular operation in space or on a lunar or planetary surface. The velocity and direction of motion which he or his extravehicular maneuvering unit impart to his body might be misjudged, causing him to strike the spacecraft, especially protrusions from its surface, with sufficient velocity to produce injury in spite of the cushioning effect of his inflated space suit. Possible injuries expected in this case are contusions and fractures, especially of the ribs. Closed abdominal and thoracic injuries might also occur. There is also the danger of an astronaut being trapped between docking space vehicles or moving sections of a space station being assembled in space. As a consequence, the involved part of his body might sustain a closed crush injury of any severity, even without suit disruption.

Injury might be sustained during operations on extraterrestrial surfaces. Awkward mobility in the space suit, associated with possible balance and locomotion difficulties while walking in unfamiliar gravity environments and on unfamiliar terrain, will predispose to falls which, despite the cushioning and splinting effects of the space suit, could result in contusions, strains, fractures, and dislocations. For the same reasons, there will also be a risk of penetrating wounds, lacerations and decompression effects (Chapters 1, 2, and 3), especially if sharp or pointed tools are to be used for climbing, digging or chipping, or if an astronaut has to walk or climb over jagged terrain.

Finally, it should be noted that meteoroid penetration of the space suit might occur during extravehicular and extraterrestrial operations. As discussed in Chapter 12, single or multiple meteoroid fragments might penetrate the skin and subcutaneous tissues to any depth, producing mechanical and possible thermal tissue damage. Deep penetration by these missiles might result in serious and potentially fatal organ damage.

#### Prevention

A number of measures should be taken in order to minimize the risk

of an astronaut being injured by mechanical forces during operations in space and on lunar and planetary surfaces. The need to keep design engineers and astronauts continually aware of this area cannot be over-emphasized. It is also important to point out that the astronaut who maintains himself at peak physical condition while in space will keep the risk of certain injuries, such as strains and sprains to a minimum.

Hazardous projections into the spacecraft cabin must be eliminated. Necessary projections must be shielded or padded, or have their edges and corners rounded. All detachable items of equipment and other material must be firmly fixed to or enclosed in fixed structures when not in use. Materials with low mass and fragmentation potential must be used whenever possible. Consideration must be given to providing optimum vehicular protection from meteoroid penetration and personal protection from penetrating fragments in various parts of the spacecraft cabin during high risk phases of a mission. Compartmentalization of the spacecraft cabin could be a measure affording protection from mechanical injuries in instances of meteoroid penetration and "explosive" decompression. All hatches on all spacecraft should be designed and standardized to facilitate rescue of injured crew members. Astronauts must be trained in rescue operations.

An astronaut should limit uncontrolled "free-floating" movements about the spacecraft cabin as much as possible. During such movements, the wearing of comfortable light-weight protective equipment such as a helmet, possibly with an attached faceguard, and a rib protector might be indicated. An astronaut should be restrained in the cabin during all spacecraft maneuvering, docking, and landing operations. When the risk of meteoroid penetration and "explosive decompression" is increased, an astronaut should don a space suit and be restrained. Hazards associated with possible servicing and repair procedures on board the spacecraft should be recognized. Procedures should then be outlined and measures taken to ensure that they will be carried out safely.

Several measures should be taken to minimize the risk of mechanical

injuries during extravehicular operations in space. Astronauts should be provided with an adequate propulsion system and be thoroughly proficient at maneuvering in space before attempting major tasks. Close attention must be given to minimizing hazards presented by projections from the surface of the spacecraft, particularly in the hatch area. An astronaut must exercise extreme caution to avoid getting crushed between docking space vehicles or moving sections of a space station being assembled.

During extravehicular operations on lunar and planetary surfaces, an astronaut must exercise extreme caution in walking and climbing over unfamiliar and rough jagged terrain. He might use a mechanical support to assist his balance and locomotion, hence preventing falls. Anchor or safety ropes might be used in certain circumstances. Extreme care must be taken in handling sharp and pointed tools.

Finally, it is assumed that an astronaut will be provided with as durable a space suit as possible. A suitable external protective garment might be indicated in various situations.

### Diagnosis

The diagnosis of a mechanical injury in space will be made primarily by history and physical examination. The history must be centered on eliciting symptomatology in detail and the mechanism of injury. The physical examination must be thorough, determining both the extent and severity of tissue damage and assessing the astronaut's total response to the injury. Periodic monitoring of his vital signs is indicated if serious bleeding has occurred or is suspected, or if he is in respiratory distress. If possible on board the spacecraft, basic laboratory and x-ray studies will be useful in confirming and diagnosing injuries.

### Treatment

Basic surgical principles will still apply to the treatment of mechanical injury in space. In the foreseeable future, definitive surgical procedures in space will undoubtedly be limited mainly to wound closure, and closed reduction of fractures and dislocations. Thus, in certain cases,

anatomical reconstruction of damaged tissues will have to be done after return to Earth. Due to weight penalties imposed by transporting stored, fresh whole blood into space, only reconstituted plasma or a suitable plasma-expanding agent such as dextran might be available for replacement of blood loss. It is apparent, therefore, that all minor mechanical injuries should be adequately treated in space. On the other hand, limitations placed on the surgical, and possibly the supportive treatment of major mechanical injuries will be such that the duration and degree of functional impairment and the mortality from these injuries will on the whole be much greater in space than on Earth.

Although the processes of repair are fundamentally the same in all body tissues, tissue differences in ability to survive and regain function following various types of damage will make each wound an individual problem in treatment. It is of utmost importance, therefore, to have a sound knowledge of the healing potential of various types of wounds and of the factors that enhance or impede healing. Above all, one must be cognizant of the serious consequences which can result if a wound should become secondarily infected.

Local and regional anesthesia for the repair of wounds in space is considered ideal in the light of the greater weight penalties and problems with atmospheric contamination which would be associated with the administration of a general anesthetic in space. Such might also be used instead of analgesic and sedative drugs if the astronaut must be maintained at an optimum functional capacity.

The immediate care of an injured astronaut must be directed at controlling bleeding, ensuring an adequate airway, and preventing "shock", further tissue damage, and further contamination of an open wound. External bleeding can, in most cases, be arrested by a sterile compressive dressing. As a rule, a well-padded tourniquet should be applied only when a major vessel in an extremity is severed, and should not be removed until definitive treatment of the wound has been instituted. Adequate ventilation of an unconscious astronaut might be attained by inserting a suitable mouthpiece. The respiratory distress associated with a chest injury

such as single or multiple rib fractures may be aided by stabilizing the involved area of the chest wall with strapping or infiltrating the appropriate intercostal nerves with a local anesthetic agent, such as 2 percent lidocaine. If these measures fail or are likely to fail, tracheostomy might be indicated. Sucking wounds of the chest must be securely closed with an airtight dressing. The atelectatic tendency in a 100 percent oxygen atmosphere makes rapid treatment of a sucking wound mandatory.

The general condition of an injured astronaut should be allowed to stabilize before definitive treatment of his injury is commenced. Blood loss should be replaced with colloid or whole blood, if available. If a large crew is on board a spacecraft, use of donor blood from other crew members whose whole blood is known to be compatible might be possible.

As pointed out in Chapter 10, cardiovascular adaptations to weightlessness will take place during prolonged space missions. A temporary, and possibly persisting decrease of blood volume will occur. Thus an astronaut who suffers from blood loss in space will in essence not receive the benefit of the "transfusion" of pooled blood if he was rendered recumbent due to blood loss prior to leaving Earth. It is thought that cardiovascular mechanisms which compensate for blood loss should not be altered by weightlessness. Since cardiovascular adaptations to weightlessness reduce orthostatic tolerance, "shock" might result from a relatively minor blood loss if measures (Chapter 10) are not taken to adequately protect an astronaut from orthostatic intolerance on return to a gravity environment.

### Closed Wounds

Even though the skin remains intact following non-penetrating trauma, any underlying tissue in the body can be damaged. Closed injuries are characterized by the tearing and crushing of soft tissues, fractures and dislocations. From previous discussion, it appears that the majority of closed injuries in space will be contusions, sprains, strains, fractures, and dislocations, of which most will not be life-threatening. On the other hand, violent non-penetrating blows might produce potentially fatal organ disruption and internal hemorrhage.

Contusions are usually produced by direct blunt force and crushing

trauma. Usually only subcutaneous tissues are injured. Small blood vessels are torn and bleed into interstitial spaces. Exudation of serum into the damaged tissues enhances swelling. When muscle is contused, a large vessel might be torn, resulting in profuse hemorrhage and possibly "shock". Extravasated blood may collect between layers of tissues to form a hematoma. Bleeding may also occur into a joint or tendon sheath to irritate and produce inflammation of these structures. An expanding hematoma may produce enough ischemia of skin and pressure on surrounding tissue to cause necrosis and secondary infection. Minor superficial contusions are swollen, tender and usually produce no loss of function. On the other hand, bleeding into a muscle, joint or tendon sheath can produce a severe restriction of movement and pain. A contused nerve in which the axons are not disrupted (neurapraxia) will be associated with temporary pain, paresthesia and paralysis in the nerve distribution, whereas disruption of axons (axonotmesis), usually occurring in association with a closed fracture, results in complete motor and sensory paralyzes which recover completely over a period of weeks to months.

The majority of the contusions discussed above are treated by non-surgical measures which are directed first at controlling bleeding, and later at hastening the resolution of the residual hematoma and edema, and restoring the injured part to optimum function. The immediate application of a suitably padded compression bandage over the site of contusion may have some effect in limiting the initial extravasation. If possible, cold compresses might also be effective, especially in areas which are superficial and not easily bandaged. Activity should be curtailed insofar as is practical until an astronaut is over the period of acute local tenderness.

Rarely is it necessary or advisable to evacuate a large superficial hematoma either to hasten return of function or prevent skin necrosis. Evacuation may be accomplished in the first few hours by needle aspiration, or if this is not possible, owing to clotting, by expressing it through a small incision made under local anesthesia. Following these procedures, a pressure dressing must be applied to prevent recurrence of the hematoma. One might also consider aspirating blood from a joint, especially the knee, for the relief of pain. It is important to point out that a definite



risk of introducing infectious organisms into damaged tissues must be assumed when carrying out the above procedures.

To assist the absorption of hematoma and edema fluid, the affected part should be placed at rest and, if possible in space, heat applied periodically. Graduated activity of the part should be commenced when deemed feasible. Recent interest has been focused on the use of orally administered and locally injected protease (plasminogen)-activating enzymes, such as combined streptokinase-streptodornase, to assist absorption of hematoma and edema fluid (2, 6, 12, 13). Whether agents presently in use significantly ameliorate symptoms and shorten recovery time remains open to question, however.

Tearing of ligaments is defined here as a sprain, and tearing an avulsion of muscle or tendon as a strain. These injuries are caused by either direct or indirect violence, and vary from incomplete to complete disruption of the continuity of these tissues. The resulting pain, swelling and loss of function are dependent upon degree of tissue damage.

The initial treatment of sprains and strains is similar to that for contusions. An analgesic or sedative might be required for pain. If an astronaut must be kept at an optimum functional level, local or regional anesthesia might be used instead of these drugs. Placing these injuries at rest is essential until healing is well progressed. In most cases, bandaging or strapping should provide adequate support. Splinting, as used for the treatment of fractures, might be required for more serious injuries, especially those which would be treated on Earth by operative repair. Graded activity, with care to avoid placing undue strain on healing tissues, should be commenced as dictated by clinical judgment.

Fractures and dislocations are also caused by direct or indirect force. A fracture can be "closed" or "open", depending on whether or not there is a communication between the site of fracture and the outside air through the skin or mucous membrane. It may be incomplete (e. g., fissure, depressed, puncture, and greenstick fractures) or complete (e. g., simple, comminuted, impacted, compression and avulsion fractures).

Fracture fragments may or may not be displaced. In addition to a fracture lesion or dislocation, there may be associated injuries to contiguous nerves, joints, tendons, and viscera. The possible existence of multiple fractures at different levels in the same bone or in other bones, or a combined fracture-dislocation must always be kept in mind. The degree of incapacitation of an astronaut will depend on the site and nature of the fracture or dislocation and the amount of associated soft tissue damage.

Careful handling of an obvious or suspected fracture or dislocation is mandatory to prevent fracture displacement, further soft tissue injury and the possible creation of an open fracture. For quick efficient temporary immobilization of an extremity fracture, a suitable pneumatic splint might be used <sup>(7)</sup>.

A displaced fracture should be reduced into as best alignment as possible in space by traction and manipulation. Ideally, reduction might be most easily and painlessly accomplished during the period of local numbness and paralysis which usually lasts for many minutes after injury. However it might be delayed if an astronaut requires resuscitation, treatment of more serious injuries or debridement of damaged tissues associated with an open fracture. If analgesia is required, an injection of local anesthetic into the fracture site might control pain until reduction is accomplished. More preferable, however, is the use of regional anesthesia, which provides both analgesia and muscular relaxation and eliminates the risk of introducing infection into the fracture site.

The treatment of open wounds with underlying fractures should be similar to that to be discussed for all open wounds. Because of the serious consequences of infection of a fracture site, a suitable broad spectrum antibiotic should be administered prophylactically for a period of time to all open fracture cases.

Complete immobilization of most fractures is essential for their healing. The type of immobilization employed will depend on the site and nature of the fracture and the availability of materials which can be used for such a purpose in space. If specific lightweight materials for

splinting or encasing fractures are not carried into space, a suitable splint might be fashioned from expendable or repair materials on board the spacecraft. Some fractures can be suitably treated by methods other than splinting or encasement. For example, adhesive strapping can be used to immobilize fractures of the clavicle, upper humerus, mandible or ribs. Other fractures may require no specific treatment except rest and perhaps temporary bandaging to minimize associated bleeding, give protection and relieve pain. It is noted that rib fractures frequently require only the relief of pain by infiltration of the appropriate intercostal nerves with a local anesthetic. Finally, it is pointed out that treatment facilities in space in the foreseeable future will be such that open reduction and internal fixation of fractures will not be possible.

Any dislocation should be reduced as soon as possible in order to minimize injury of contiguous structures, especially nerves and blood vessels. Regional anesthesia might be of great benefit by providing temporary relaxation of muscles as well as analgesia around the dislocation. Complete immobilization of the joint for several weeks might be required to allow healing of torn joint structures. Otherwise, movement might be restricted for a short period of time, followed by a graded activity as indicated.

Violent trauma can produce a great variety of closed injuries of a more serious nature than those discussed above. Of particular concern are the consequences of severe blows and crushing forces, especially in the head and thoracoabdominal regions. These forces can disrupt underlying viscera and supporting structures leading to serious internal bleeding. It is important to point out that many serious closed injuries can occur not only in the absence of early or obvious external signs of violence, but also far removed from the site of external impact.

A blow to the head can produce concussion or unconsciousness due to functional or anatomic derangement of the brain stem. It is noted that concussion, brain contusion or laceration, and skull fracture may occur singly or in any combination <sup>(5)</sup>. Consciousness may return within

seconds following concussion or may take minutes to days following more serious brain injury. Cases which recover slowly pass through a transitional state of semi-consciousness characterized by disorientation and confusion which are attributed mainly to cerebral edema. Common complaints during this period are severe headache, lightheadedness or vertigo, and nausea and vomiting. Permanent residual psychologic and motor defects may result from anatomic damage to the brain. A delayed deterioration of consciousness or a deepening coma may occur following head trauma, due to an enlarging intracranial mass such as an extradural, subdural, or intracerebral hematoma, to a subdural collection of cerebrospinal fluid, or to cerebral edema. Deterioration due to expansion of a chronic subdural hematoma may follow a lucid interval of several days to a few weeks, even after a seemingly minor blow to the head. Fractures through the temporal region may affect vestibular function possibly resulting in severe vertigo, nausea, and vomiting. Open skull fractures, especially those associated with dural laceration, may discharge cerebrospinal fluid and allow the entry of infectious organisms to produce meningitis, osteomyelitis, cerebritis, or brain abscess.

A severe blow or crushing injury of the chest may produce a hemothorax. A fractured rib can penetrate the lung to produce a pneumothorax with or without associated bleeding. The pneumothorax may be of the "tension" variety in which the passage of air back out of the pleural cavity is blocked by the flap of torn lung pleura which acts as a ball valve, so leading to serious pulmonary and cardiovascular insufficiency. Air escaping from the disrupted lung may dissect along bronchovascular roots of the lung into the mediastinum to produce mediastinal emphysema. It may even track into the neck, face, scalp and thoracic wall to produce subcutaneous emphysema. This condition becomes serious when air within the mediastinum produces an acute restriction of venous return to the heart or when secondary mediastinal infection occurs. Severe blows over the cardiac region of the chest may contuse the heart, resulting in a clinical condition not unlike that of coronary artery occlusion with myocardial infarction.

A blunt force to the abdominal region can contuse or lacerate solid viscera, or rupture hollow viscera. All types of abdominal injury, regardless of the organ injured, may produce two primary effects - "shock" and "peritonitis" - either singly or together. A fixed organ is more likely to be injured than one which is more mobile. Organs frequently injured on Earth, in approximate order of frequency, are liver, spleen, small bowel, large bowel, kidneys, stomach, urinary bladder, and diaphragm (left side) <sup>(8)</sup>. Certain parts of the small intestine are much more prone to injury, such as the third part of the duodenum, the proximal jejunum and the distal ileum. Delayed intra-abdominal hemorrhage may occur from a damaged spleen, liver duodenum, pancreas, or kidney. It is noted that closed abdominal injuries usually present a particularly difficult problem in early diagnosis, for the initial trauma may be remarkably trivial and a severe blow to the abdomen may be followed by rapid recovery and an interval of several hours, and rarely days without implicating signs and symptoms before the actual injury becomes clinically manifest.

As was previously pointed out, definitive surgical procedures in space in the foreseeable future will be limited mainly to wound closure and closed reduction of fractures. Thus the treatment of serious closed injuries will be supportive. Intravenous fluids and electrolytes to maintain water and electrolyte balance, fluids such as plasma, a plasma expanding agent, or whole blood for blood loss, analgesic drugs for the control of pain, and a suitable broad spectrum antibiotic for the prevention and control of infection are considered the most essential forms of therapy to have available in space. Numerous other supportive measures are conceivable. A cerebral dehydrating agent such as mannitol might be used for relieving post-traumatic cerebral edema or preventing post-traumatic renal tubular necrosis. An ataractic drug, such as sodium phenobarbital, might be administered to control agitation associated with brain injury. A tracheostomy might be performed to improve lung ventilation. The removal of air or blood from the pleural cavity might be accomplished by periodic needle aspiration or, in a case with severe bleeding or "tension" pneumothorax, by continuous

suction. Acute restriction of venous return to the heart due to mediastinal emphysema might be relieved by an incision made under local anesthesia at the base of the neck. Cardiovascular drugs such as a rapid-acting cardiac glycoside (e.g., digoxin) or a vasopressor agent (e.g., metaraminol) might be administered to cases which develop myocardial insufficiency due to cardiac contusion. Nasogastric intubation might be necessary to relieve upper gastrointestinal distension or vomiting, decompression of the upper gastrointestinal system, or for feeding. An indwelling urinary bladder catheter might be required for bladder drainage in an unconscious astronaut or to decompress a damaged urinary tract. Finally, even though the view is held that definitive surgery will not be performed in space in the foreseeable future, it is considered possible that physician-astronaut might, under certain circumstances, make a heroic operative attempt to save a fellow astronaut's life using the limited instruments available. Some operations which come to mind are trephining, splenectomy, amputation, and repair of a disrupted hollow or solid abdominal viscus.

### Open Wounds

Open wounds denote a break into or an actual loss of the protective skin barrier, with the underlying tissues being damaged to varying degrees and extent. As compared to closed injuries, open wounds are subject to contamination by bacteria introduced into the wound by the wounding agent or by foreign material.

The various types of open wounds include abrasions, lacerations, penetrating injuries, avulsions and crushing injuries. The degree of damage to deeper tissues is often suspected from the nature of the trauma and the type of wound produced. Injured nerves, muscles and tendons in wounds involving the extremities can usually be diagnosed by testing the function of parts distal to the site of injury. On the other hand, the ultimate extent of injury in penetrating injuries of the neck, thorax, and abdomen may not be obvious. No wound in any location should be probed in an attempt to establish the extent or depth of injury, for this maneuver cannot be expected to yield reliable information and can cause further

harm by accentuating hemorrhage and introducing further contamination.

An abrasion is the most superficial type of open wound, with only the skin being destroyed to a variable depth. Slight bleeding and serum exudation occur from the injured surface and form a thin eschar under which the denuded epithelium regenerates. If infection supervenes, healing is delayed.

A laceration is a linear wound in which the skin and underlying tissue damage are localized to the path of the wounding agent, which can be either a sharp or blunt object. It may vary from a neatly incised defect to one with irregular torn and contused edges with much associated tissue loss.

A penetrating wound is created by a missile or sharp object which might pass to any depth into or right through tissues. The greater the velocity of the penetrating agent, the less the likelihood of skin or clothing being carried into the wound by the agent. Due to its mass and velocity, a penetrating agent may dissipate enough kinetic energy in its passage to produce extensive tissue damage around the wound tract. Of note is the fact that in perforating injuries from high velocity missiles, wounds of exit are usually larger than those of entrance. Thus it is conceivable that in the space situation, a penetrating, high velocity, dense meteoroid or spacecraft wall fragment might conceivably damage blood vessels, nerves and other tissues at varying distances from the course of the "missile", with the external appearance of this serious wound being quite misleading. That even more widespread tissue damage might be caused by bone and "missile" fragments is also possible. Reference is made to further discussion of injuries due to meteoroid penetration in Chapter 12.

Avulsions are characterized by the tearing of tissues from their attachments. Skin and subcutaneous tissues can be either partially or completely avulsed from underlying tissues. Any degree of extent of damage to deeper structures can occur. A torn flap may or may not remain viable, depending on the adequacy of its blood supply.

Open crushing wounds can be present with any combination of the various types of open wounds discussed above. Open or closed damage to deeper

tissues, including bones and viscera, may be extensive.

The treatment of all open wounds in space will be governed by the same surgical principles as on Earth. The primary objective will be to convert, as soon as possible, an open contaminated wound into a surgically clean, closed wound. There is a generally accepted optimal time or so-called "golden period" of eight hours during which, from the standpoint of minimizing bacterial invasion of tissues, wound care should be undertaken. However there may be many other factors, such as wound blood supply, and devitalization and contamination of tissues which have to be taken into consideration other than such an arbitrary time limit. If wound care must be delayed until an astronaut's general condition is stabilized or a more serious injury is treated, the wound should be covered with a sterile compressive dressing to minimize further contamination and bleeding. It is noted again that as a rule, a well-padded tourniquet should be applied only when a major vessel in an extremity is severed, and should not be removed until definitive treatment of the wound has been instituted. Whether local or regional anesthesia will be used during wound repair in space will depend upon the nature of the wound.

Wound cleansing, using aseptic precautions (sterile surgical gloves, surgical mask, etc.,) is the first step in definitive open wound treatment. After carefully cleansing the surrounding skin with an antiseptic agent (e.g., hexachlorophene soap) and possibly shaving off hair, it may be necessary to irrigate the wound with a suitable sterile solution (e.g., isotonic saline) and remove loose foreign material. Droplet contamination of the spacecraft cabin atmosphere might be avoided by keeping a sterile absorptive material and strong suction device in close proximity to the wound, or by completely enclosing the wounded area in a container which might be used for washing purposes in space. Draping the wound from unprepared skin surfaces might be accomplished with a sterile adhesive material, or by the circumferential application or tying down of a sterile nonadhesive material.

The next step in definitive wound treatment in space will be to make the wound as surgically clean as possible. This goal is accomplished by debriding or removing devitalized tissues, foreign substances and tissues



which are hopelessly damaged, so leaving a wound which contains only viable tissues with an adequate blood supply. It may be necessary to enlarge a wound in a suitable line to display the full extent of damage. Each type of tissue encountered must be removed only after a careful intelligent evaluation of its viability, for there must be no needless sacrifice of tissue. Blood clots must be removed and careful hemostasis achieved.

The repair of wounds in space will be limited mainly to wound closure. On the other hand, it is considered possible that an experienced physician-astronaut might undertake in space, when indicated, nerve, blood vessel, and tendon repairs with appropriate suture materials.

Every open wound in space should be closed if at all possible, providing that undue tension does not have to be placed on the tissues. Minimal skin tension might be relieved with subcutaneous sutures or by making relaxing incisions. Suturing with a fine, non-reactive material still remains the best all-around technique for skin closure. Experimental and clinical success has recently been reported in closing skin with a sterile surgical adhesive tape (3, 4, 11). Although such a tape is highly recommended for use in space, it is probable that tape methods of skin closure will never completely replace suture methods, especially in moist, oily or highly mobile surface areas, or for closing jagged or sharply angulated wounds. It appears that where a broad defect exists, taping can oppose skin edges which would otherwise be closed only after undermining of the skin or making relaxing incisions.

After wound closure, a generous dressing must be applied and, if necessary, the part immobilized to promote healing and prevent infection. Broad spectrum antibiotics might be administered prophylactically where there is a high risk of a contaminated wound becoming infected.

Finally it should be mentioned that due to extensive tissue loss, post-traumatic swelling or severe contamination, primary closure of a wound may not either be possible or advisable. The wound must then be packed with fine mesh gauze or other suitable material, a generous dressing applied and the affected part splinted. So-called delayed primary closure of a wound, if clean, should then be attempted in about five

to seven days. If a wound becomes infected or if the defect is too large to close, one will have to allow it to close by granulation, or by so-called "secondary intent". Repeated dressing changes and continued support of the part will be required until healing is complete. Antibiotic therapy should be administered to infected wound cases.

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## CHAPTER 15

### CARBON DIOXIDE (CO<sub>2</sub>) TOXICITY

Astronauts risk exposure to a toxic level of CO<sub>2</sub> during space missions. An accumulation of this waste product of body metabolism could occur in the atmosphere of a spacecraft cabin or space suit due either to a partial to complete failure or a temporary overloading of a CO<sub>2</sub>-absorbing system.

Fortunately an astronaut's inspired CO<sub>2</sub> can be prevented from reaching a toxic level in a number of ways. Environmental control systems can be designed to handle all possible peak CO<sub>2</sub> loads. The reliability of these systems can be increased with emergency subsystems which either absorb CO<sub>2</sub> or purge atmospheres of this gas. As well, breathing gas can be supplied directly to an astronaut if he is exposed to a toxic ambient CO<sub>2</sub> level.

Although adequate measures will presumably be taken to prevent the occurrence of CO<sub>2</sub> toxicity in space, it is still considered possible that such measures could become inadequate, especially during prolonged missions and particularly strenuous extravehicular operations. For example, if failure of a CO<sub>2</sub>-absorbing system occurs, atmospheric purging or breathing oxygen from an open loop system might have to be limited, and so some elevation of atmospheric CO<sub>2</sub> tolerated, in order to conserve oxygen. Accordingly, it is necessary to consider the medical consequences of such a situation and determine what therapeutic measures might be taken in space to combat CO<sub>2</sub> toxicity and so maintain an astronaut's performance capacity at an optimum level.

This chapter presents various aspects of CO<sub>2</sub> toxicity considered pertinent to the space situation. It will become apparent that differences between the short and long term effects on man, and between the possible circumstances of exposure to CO<sub>2</sub> in space dictate the necessity to discuss this area under the separate headings of "Acute CO<sub>2</sub> Toxicity" and "Chronic CO<sub>2</sub> Toxicity".

Also by way of introduction, it should be pointed out that virtually all

studies in the past have stated inspired  $\text{CO}_2$  levels as "percent" rather than as "partial pressure". The partial pressure of  $\text{CO}_2$  actually determines pathophysiologic effects of this gas. It also remains constant as the percent composition of this gas changes for different space atmospheres and will probably be sensed by all space atmospheric monitoring systems (35, 134). Hence the use of this unit is definitely preferable, especially when recommending maximum allowable levels of  $\text{CO}_2$  for space atmospheres.

An accurate conversion of percent  $\text{CO}_2$  data stated in the literature to partial pressure values will not be attempted in this chapter, for few investigators have made note of ambient atmospheric pressure, temperature, and relative humidity. However, most of the information involving the inhalation of  $\text{CO}_2$  has given the inhaled dry air percentages of  $\text{CO}_2$ . It is thought that atmospheres of past experiments can be reasonably well approximated by assuming a sea level pressure of 14.7 psia (760 mm Hg). Hence a partial pressure of  $\text{CO}_2$  of about 7.5 mm Hg would represent one percent  $\text{CO}_2$ .

A physiological basis of comparison is the partial pressure of tracheal  $\text{CO}_2$ . This value is stated in terms of body temperature, at ambient atmospheric pressure in air saturated with water vapor (BTPS). The relationship of the partial pressure of tracheal  $\text{CO}_2$  and barometric pressure (or altitude) for various sea level equivalent percentages of  $\text{CO}_2$  is shown in Figure 15.1.

In this chapter,  $\text{CO}_2$  levels will still be stated conventionally as percent, but whenever exposure of an astronaut to  $\text{CO}_2$  in space atmospheres comes into consideration, partial pressures of  $\text{CO}_2$  equivalent to concentrations in the sea level atmosphere defined above will also be stated.

#### Acute $\text{CO}_2$ Toxicity

Broadly speaking, acute  $\text{CO}_2$  toxicity denotes the effects suffered by an astronaut who is exposed to toxic atmospheric  $\text{CO}_2$  levels which are reached within and persist at varying and maintained levels for minutes to as much as 24 hours in duration. An acute toxic condition in this case differs considerably from one resulting from a more prolonged, or chronic

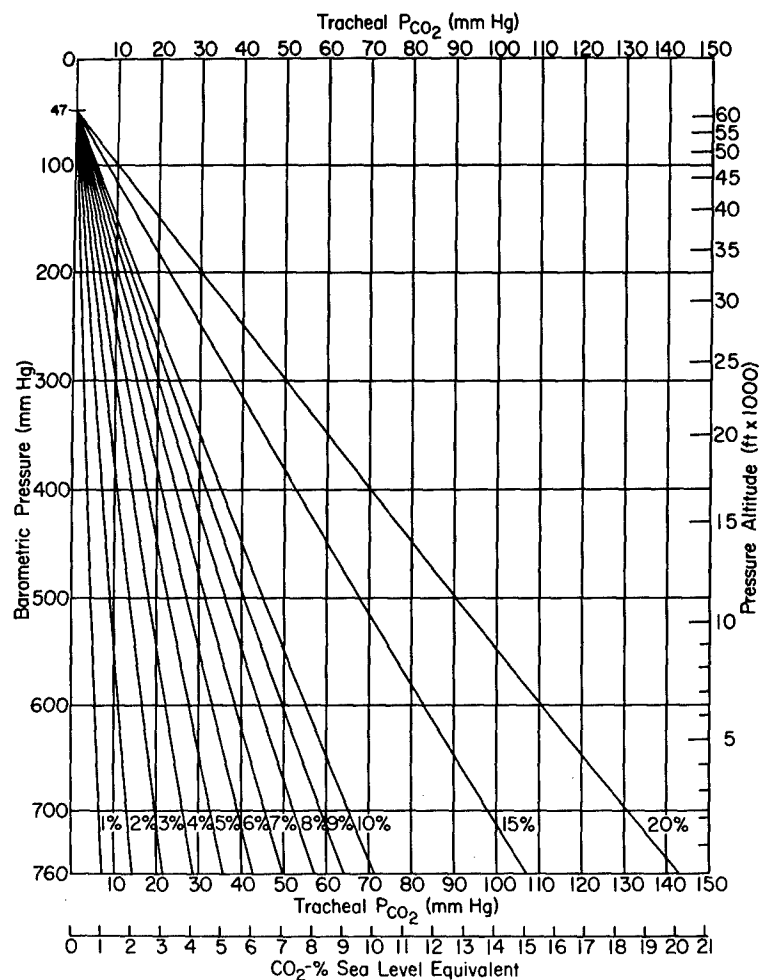


Figure 15.1 Relationship of partial pressure of tracheal  $CO_2$  and barometric pressure (altitude) for various sea level equivalent percentages of  $CO_2$ .

(After Luft (124)).

exposure to  $CO_2$ . It could arise from a temporary  $CO_2$  build-up in cabin or suit atmospheres due to inadequate functioning of life support systems.

The accumulation of  $CO_2$  will obviously be much faster in a space suit than in a spacecraft cabin atmosphere. Rough calculations based on current suit data indicate that an astronaut who is walking on a lunar or planetary surface can increase his inspired  $CO_2$  to a highly toxic level, as will be defined below, within one to two minutes after a complete cessation of  $CO_2$  absorption by his extravehicular life support system (134, 175).

It is noted, however, that CO<sub>2</sub> storage by the body would have a significant retarding effect on rates of atmospheric CO<sub>2</sub> accumulation only in such a small rebreathing volume as that in a space suit (60, 61, 68, 169). In fact, recent evidence indicates that the immediate storage of CO<sub>2</sub> involves a body compartment with a volume corresponding to that of the extracellular space (68, 147). Carbon dioxide storage by the body should therefore be taken into account when attempting to predict such rates accurately. As far as CO<sub>2</sub> accumulation in spacecraft cabins is concerned, it is estimated that three astronauts who are carrying out normal intra-vehicular operational tasks would not, even in the confined volume of the Apollo Command Module, experience symptoms of CO<sub>2</sub> toxicity until about 6 to 7 hours after CO<sub>2</sub> removal from their atmosphere ceases. From such considerations, then, one can foresee the possibility of toxic levels of CO<sub>2</sub> being reached over a period of minutes in space suit atmospheres and over a period of hours in spacecraft cabin atmospheres. Because of such a marked time difference, the question arises as to whether or not the rate of CO<sub>2</sub> increase can significantly alter an astronaut's response to acute exposures to this gas in space. Fortunately such information can be obtained from reports of past exposures of man to constant and gradually increasing levels of inspired CO<sub>2</sub>. For all practical purposes, it can be assumed that exposures to constant levels of CO<sub>2</sub> are equivalent to those that could occur over a brief period of time in a space suit.

### Pathophysiology

Since the pathophysiology of man's response to acutely elevated partial pressures of CO<sub>2</sub> in his inspired air is well documented in the literature, it will receive only brief attention here. Particular emphasis will be placed on those aspects which are considered practical from a space operational standpoint and pertinent to ensuing discussions of the clinical manifestations, diagnosis, prevention, and treatment of acute CO<sub>2</sub> toxicity in space. Greater detail in this area is provided by the references to be cited.

Carbon dioxide is a powerful stimulus to breathing. This is an effect



which, within limits, is the major factor protecting man from acutely elevated, otherwise toxic concentrations of this gas in his ambient atmosphere. The increase in pulmonary ventilation produced by  $\text{CO}_2$  varies markedly at different times in a normal individual and throughout the normal population (55, 93, 100, 188, 223). The population response characteristic appears to account to some degree for variations in tolerance to  $\text{CO}_2$ , for it has been demonstrated that individuals with a relatively large tidal volume and slow respiratory rate show less of a respiratory and sympathetic nervous system response, and less symptoms while breathing low concentrations of  $\text{CO}_2$  than individuals with a relatively small tidal volume and fast respiratory rate (178, 188). Accordingly, knowledge of responses to  $\text{CO}_2$  might have some practical value from a monitoring standpoint.

An average effect of various inspired air- $\text{CO}_2$  mixtures upon the steady state alveolar minute ventilation and partial pressure of  $\text{CO}_2$  of normal resting man at sea level is shown in Figure 15.2. This response curve, which can be calculated from equations developed by Gray (84, 85), correlates well with other data in the literature (29, 67, 82, 98, 100, 171, 188, 223). It demonstrates the increasingly inadequate ventilation, notably paralleled by an accelerating rise of alveolar  $\text{CO}_2$ , as the ambient  $\text{CO}_2$  increases. This dulling of man's ventilatory response to progressively increasing levels of  $\text{CO}_2$  has been attributed to a combination of the narcotic effect of  $\text{CO}_2$  on respiratory center neurons, the stimulation of pressure receptors in the thorax by hyperventilation and the fatiguing of respiratory muscles (41, 55).

Much research has failed to adequately define the mechanisms by which an increase in inspired  $\text{CO}_2$  produces an increase in pulmonary ventilation (91, 112, 114). A few aspects of this area are pertinent to this discussion. For greater detail, the excellent reviews by Hamilton and Brown (91), Heymans and Neil (96), Kellogg (102), Tenney and Lamb (212) and others (40, 51, 52, 85, 88, 99, 113, 120, 155, 211) can be consulted.

It has been observed in humans, and substantiated by animal experimentation, that breathing 100 percent oxygen at pressures near sea level for short periods of time significantly depresses respiratory reactivity to  $\text{CO}_2$ , presumably through the effects of oxygen on peripheral chemoreceptor sensitivity for  $\text{CO}_2$  (19, 91, 113, 114, 121).

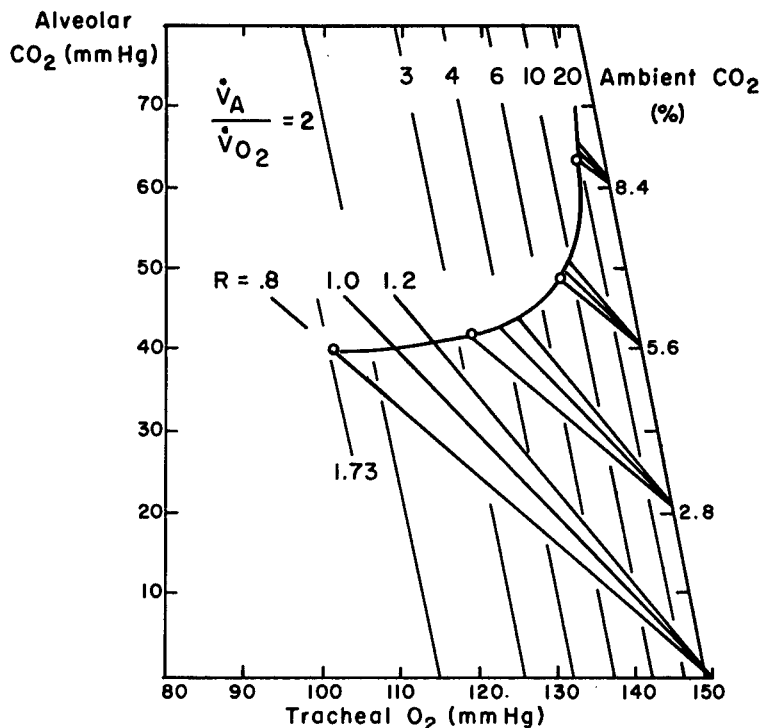


Figure 15.2 Effect of inspiring various CO<sub>2</sub>-air mixtures upon the steady state alveolar gas composition of normal man at rest. The ratio  $\dot{V}_A/\dot{V}_{O_2}$  represents liters (BTPS) per minute of O<sub>2</sub> alveolar ventilation for every 100 ml(STPD) of oxygen consumed per minute. R represents the respiratory exchange ratio (volume of CO<sub>2</sub> output for volume of O<sub>2</sub> intake) and would be equal to the respiratory quotient (RQ) under steady state conditions at sea level.

(After Fenn (64, 65)).

This effect was not found, however, when a few individuals were exposed to 100 percent oxygen at an atmospheric pressure of 200 mm Hg for 4 days, or when sleeping subjects near sea level breathed 40 to 100 percent oxygen for periods of 40 minutes to a few hours in duration (34, 47). The reason for these divergent results cannot be given. As far as the potential exposure of an astronaut to increased levels of CO<sub>2</sub> is concerned, studies of man's response to CO<sub>2</sub> in various possible space atmospheres which contain oxygen above that breathed on Earth appear indicated. As well, it is

deemed advisable to assess this response in atmospheres containing inert gases which are being considered for use in space.

The ventilatory responsiveness to  $\text{CO}_2$  is initially increased on exposure to altitude, or exposure to lowered partial pressures of oxygen (200, 214). It then returns to normal over the period of several days required to acclimatize to the altered atmosphere (200, 214). The finding that a reduction of cerebrospinal fluid bicarbonate occurs during acclimatization points to the importance of the fluids in which the respiratory neurons are bathed in governing central chemoreceptor activity (112, 200).

The observation that the ventilatory response to inspired  $\text{CO}_2$  lags changes in alveolar  $\text{CO}_2$ , which consistently overshoots or undershoots its steady state value, has been attributed to the time taken for  $\text{CO}_2$  in tissues surrounding central chemoreceptors to equilibrate with altered blood  $\text{CO}_2$  (73, 88, 158, 171). This lag effect might result in a hypocapnia sufficient to produce the clinical manifestations which can accompany  $\text{CO}_2$  withdrawal (188).

The question arises as to whether or not an increasing level of  $\text{CO}_2$  in an astronaut's ambient atmosphere could actually confer some protection on him from decreasing otherwise hypoxic levels of oxygen. It has been suggested in theory and established empirically that by stimulating ventilation with a proper amount of  $\text{CO}_2$  in the inspired air, the alveolar oxygen tension can be somewhat increased, and so performance and well-being at moderate altitudes maintained (123, 161, 194, 210). However, since the major factors underlying this phenomenon are the displacement mainly of nitrogen in alveolar air by  $\text{CO}_2$ , with an associated elevation of the alveolar oxygen tension due to increased ventilation, it is readily apparent that  $\text{CO}_2$  can not confer any protection from hypoxia in a pure oxygen space atmosphere (123). Moreover, it is doubtful if this effect could exist to a significant degree in proposed space atmospheres, which have a much lower inert gas concentration than air (124).

Although it has not been shown by some investigators, there appears to be a significant decrease of man's respiratory responsiveness to  $\text{CO}_2$  with increasing depth of natural sleep (10, 16, 34, 126, 170, 173). As well, there is an associated respiratory depression resulting in an

elevation of alveolar and hence arterial  $\text{CO}_2$  (10, 16, 17, 34, 66, 73, 173). One group of investigators recorded a peak alveolar  $\text{CO}_2$  increase averaging 9 mm Hg in 14 subjects who were in deep sleep not assisted with a hypnotic drug (16). Since the majority of normal individuals studied remained asleep until their ambient  $\text{CO}_2$  reached 4 percent or their alveolar  $\text{CO}_2$  reached 50 mm Hg, one wonders, therefore, if an astronaut exposed to an increasing level of inspired  $\text{CO}_2$  while asleep might on awakening suffer from the clinical manifestations which can accompany  $\text{CO}_2$  withdrawal (16, 34, 173).

An elevated level of inspired  $\text{CO}_2$  can lead to a decrease in body temperature, even in a comfortable or warm high humidity environment (28, 32, 90). For example, Brown (28) recorded a 1 to 3° F decrease in body temperature, with associated chilly sensations, during, and for many minutes after their subjects ceased breathing about 5 percent  $\text{CO}_2$ , which accumulated in their 72° to 77° F environment over a period of several hours. This lowering of the body heat store may be due to a combination of a number of  $\text{CO}_2$  effects on the body. Increased heat loss will result from  $\text{CO}_2$ -induced cutaneous vasodilatation and hyperventilation (33, 75, 186). In the past few years, attention has been focused on the marked increase in sweating which accompanies acute exposures to toxic levels of  $\text{CO}_2$  (31, 109, 178). This phenomenon, which cannot be attributed per se to an increase in ventilatory work, may be due to one or more of several factors, such as a lowering of the thermostatic setting of the hypothalamus, an increased sensitivity of cutaneous thermoreceptors, an increase in sympathetic nervous system activity, or an augmentation of sweat gland effector activity (32). It has also been shown that toxic levels of  $\text{CO}_2$  markedly suppressed the shivering which followed exposure to a cold environment (33). In the light of the above considerations one wonders, therefore, if acutely elevated  $\text{CO}_2$  concentrations could increase an astronaut's susceptibility to cold, leading to a lowering of body temperature and associated symptoms sufficient to reduce his functional capacity or even to render him significantly more susceptible to hypothermia (Chapter 7).

A practical question that arises is whether the oxygen cost of increased

ventilation in response to elevated levels of inspired  $\text{CO}_2$ , especially if this gas is maintained at tolerable levels for a prolonged period of time, could possibly impose a significant drain on space suit or spacecraft cabin oxygen stores. In one study, the oxygen consumption of 12 normal subjects exposed to elevated concentrations of  $\text{CO}_2$  in air increased linearly by 2.3 ml per minute per mm Hg rise in alveolar  $\text{CO}_2$ , or by 1.4 ml per liter of air breathed <sup>(24)</sup>. The latter value corresponds quite well to other data on the oxygen cost of breathing <sup>(37, 38, 44)</sup>. Applying the former value to the  $\text{CO}_2$  response curve in Figure 15.2 and assuming an R of 0.8, the inhalation of 2.8, 5.6, and 8.4 percent  $\text{CO}_2$  would on the average increase the oxygen uptake by about 6, 21, and 47 ml per minute, respectively. Such data indicates, therefore, that until the inspired  $\text{CO}_2$  reaches highly toxic levels, as will be defined below, increased ventilation should place a relatively insignificant demand on oxygen stores in space systems. By the same token, it is noted that at highly toxic  $\text{CO}_2$  levels, there will also be a significant increase in  $\text{CO}_2$  output, and hence an accelerated rise of atmospheric  $\text{CO}_2$ .

Data on the effects on man of breathing various concentrations of  $\text{CO}_2$  while performing at various work loads have been confusing. In one study it was shown that 3 percent  $\text{CO}_2$  augmented the ventilatory response on commencing work, yet in another, 5 percent  $\text{CO}_2$  did not alter this response <sup>(97, 109)</sup>. Sustained work has been found to depress the threshold of the respiratory center to  $\text{CO}_2$ , presumably due to lactic acid accumulation and elevated body temperature <sup>(5)</sup>. Combined work and  $\text{CO}_2$  have reportedly had additive and multiplicative effects on ventilation <sup>(4, 111)</sup>. Craig <sup>(45)</sup> generalized from his own as well as other data that although the increment of minute ventilation produced by a change from rest to exercise is increased by  $\text{CO}_2$ , the ratio of exercise minute volume to resting minute volume is decreased by this gas. It was assumed that this effect was due mainly to a depression of the respiratory center by increasing partial pressures of alveolar  $\text{CO}_2$ .

From a space operational standpoint, however, it is important to point out that an astronaut's work capacity could be significantly limited, possibly at  $\text{CO}_2$  levels, which would not have an observable effect on him

at rest. In 1908, Hill and Flack <sup>(98)</sup> reported that the work output of a mine worker diminished when the level of CO<sub>2</sub> accumulating in his breathing apparatus passed 2 percent. It is a well known fact among submariners that dyspnea and fatigue can severely limit the performance of heavy manual tasks when the ambient atmospheric CO<sub>2</sub> concentration rapidly reaches 3.0 to 3.5 percent. Although such information is of great operational value with respect to manned space missions, the effects of various partial pressures of acutely elevated inspired CO<sub>2</sub> on man's maximum work capacity have apparently not been reported in the open literature. Instead, interest has been focused on more physiologic aspects of exercise-CO<sub>2</sub> interactions, especially on associated changes in lung ventilation.

The cause of this inordinate dyspnea and fatigue, which characteristically occur at much lower levels of ventilation than that produced by severe work or by breathing a high CO<sub>2</sub> level alone, is unknown <sup>(224)</sup>. It has recently been shown in animal experiments that the ability of the body to increase metabolism above basal levels is significantly inhibited by hypercapnic acidosis <sup>(145, 165)</sup>. Since the availability of free acids, which are the main fuel utilized by the body during exertion, is limited by acidosis, the combined acidotic effects of work and CO<sub>2</sub> breathing on this metabolic pathway might account for the lowered CO<sub>2</sub> tolerance for a given work level, and vice versa <sup>(141)</sup>.

Since dyspnea is the major symptom which limits work performance in a CO<sub>2</sub>-containing atmosphere, the ventilatory responses to low levels of inspired CO<sub>2</sub> at rest and during exercise might indicate what minimum level of acutely inspired CO<sub>2</sub> might possibly affect an astronaut's maximum work capacity. Haldane and Priestley <sup>(89)</sup> reported that during work in a closed chamber, accumulating CO<sub>2</sub> in the chamber appears to "affect respiration" at an atmospheric concentration of 2 percent, as compared to 3 percent at rest, due to increased metabolic production of CO<sub>2</sub>. Krogh and Lindhard <sup>(109)</sup> observed that the initial increase in ventilation on commencing severe exercise is markedly elevated in a 3 percent CO<sub>2</sub> atmosphere as compared to when the same degree of work is performed in air. Brown <sup>(28)</sup> noted that active exertion had a slight

effect on the respiration of his subjects when their ambient atmospheric  $\text{CO}_2$  accumulated to the 2 percent level. Data has also been compiled showing that sustained exercise can markedly lower the ventilatory threshold for  $\text{CO}_2$  <sup>(5)</sup>. Thus it is conceivable that a relatively low level of atmospheric  $\text{CO}_2$ , possibly as low as 2 percent, might degrade an astronaut's maximum work capacity significantly. Again, it is apparent that space-oriented research aimed at better defining man's work capacity at various levels of inspired  $\text{CO}_2$ , especially at maximum recommended levels of  $\text{CO}_2$  for space atmospheres, is definitely indicated.

An increase in sympatho-adrenal activity is another major physiologic response which appears to protect man from otherwise toxic concentrations of  $\text{CO}_2$  to which he is acutely exposed. It is a well established fact that up to highly narcotic levels of  $\text{CO}_2$ , an increase output of catecholamines counteracts the depression of cardiac and smooth muscle produced by the  $\text{CO}_2$ -induced acidosis and thereby prevents eventual secondary hypotension and "shock" (29, 131, 136, 144, 155, 167, 194, 198, 212). It should be remembered, however, that hypercapnic acidosis produces two antagonistic effects in the mammalian preparation (127, 129, 141, 145, 165). On the one hand, the sympatho-adrenal system is stimulated by the decrease of arterial pH. On the other hand, the functional effects of the catecholamines are inhibited, again presumably due to the lowering of pH. The net result of this antagonism on the cardiovascular system might be altered considerably by such factors as drugs, hemorrhage, plasma and fluid loss, or concomitant metabolic acidosis or alkalosis.

Many investigators have shown that systolic and diastolic blood pressures and heart rate increase when normal individuals breathe  $\text{CO}_2$ -rich mixtures (29, 55, 82, 119, 138, 188, 194, 198). In spite of earlier reports to the contrary, cardiac output also increases (3, 55, 128, 167, 194, 198). These cardiovascular events have been attributed to two actions of  $\text{CO}_2$ . First, the increase in ventilation in response to  $\text{CO}_2$  could augment venous return, and so cardiac output through the thoracic pump mechanism (3, 75, 198). This mechanism may well operate alone up to

inspired CO<sub>2</sub> concentrations of about 6 percent, and appears to exert its greatest effect when the subject is in a horizontal position, which minimizes venous pooling in the extremities (3, 82). Second and most important, Sechzer and coworkers (198) have demonstrated in normal subjects that at alveolar CO<sub>2</sub> levels above 50 mm Hg (corresponding to an inspired CO<sub>2</sub> of about 6 percent in Figure 15.2), the concentration of catecholamines and 17-OH corticosteroids in the blood begins to increase. They believe that epinephrine liberated from the adrenal medulla and norepinephrine secreted in the myocardium, together with the effects of increased respiratory effort account for the cardiovascular events produced by CO<sub>2</sub> above this level. The importance of the sympathetic response in protecting man from high concentrations of CO<sub>2</sub> is demonstrated by the fact that sympathectomized subjects respond to CO<sub>2</sub> with hypotension rather than hypertension (43, 207). The sympathetic response to CO<sub>2</sub> may also have been primarily responsible for preventing orthostatic intolerance both in subjects who breathed 4 to 7 percent CO<sub>2</sub> for varying periods of time after exercise and in quadriplegics who breathed 5 percent CO<sub>2</sub> during tilting (54, 130). Although 17-OH corticosteroids do appear to help maintain normal myocardial contractility and may also be important in regulating smooth muscle activity, their role in orthostasis has not been defined (205, 212).

It cannot be stated with certainty if CO<sub>2</sub> accumulation in an astronaut's ambient atmosphere would enhance his susceptibility to or protect him from orthostatic intolerance on return to a gravity environment, especially if he has sustained some degree of cardiovascular deconditioning during his exposure to weightlessness (Chapter 10. It is a well established fact that both CO<sub>2</sub> and exercise are vasodilatory. Accordingly, it is thought possible that this susceptibility might be significantly increased, especially when an astronaut ceases muscular activity, since the latter assists in maintaining an adequate venous return and provides some protection against orthostatic intolerance.

Finally, it should be noted that studies of the effects of intravenous buffering agents on the sympatho-adrenal response to CO<sub>2</sub> appear to have elicited the probable major mechanism by which CO<sub>2</sub> produces toxic



manifestations. The  $\text{CO}_2$ -induced changes in blood pH in animals have been buffered with intravenous sodium carbonate or an amine buffer, tris (hydroxymethyl)-aminomethane. In a study using sodium carbonate, the blood catecholamines increased, whereas in studies using the amine buffer, the blood catecholamines remained unaltered (101, 117, 118, 143, 144). Based on earlier work in this area, the difference in these observations was attributed to the fact that blood sodium bicarbonate, which increased during the sodium carbonate infusion, diffused less rapidly than  $\text{CO}_2$  into the intracellular space, whereas the amine buffer rapidly distributed itself throughout both the intra- and extracellular spaces, and thus maintained more constant intracellular bicarbonate-carbonic acid relationships (101, 117, 142, 143, 156, 174, 220). These findings suggest, therefore, that the sympatho-adrenal response to  $\text{CO}_2$  results from intracellular pH changes. Since administration of the amine produces a marked suppression of respiratory activity, it is probable that intracellular acidosis is the major mechanism of  $\text{CO}_2$  toxicity (14, 22, 27, 122, 142, 154). This action of tris (hydroxymethyl)-aminomethane will again come into consideration when its potential value in treating  $\text{CO}_2$  toxicity in space is assessed.

Natural body buffering activity does not respond rapidly enough to counteract the acidotic effects of an acute exposure to  $\text{CO}_2$  (20, 46, 53, 57, 69, 81, 152, 168, 196, 197, 212, 219). This fact was borne out well in the experiments of Schwartz and coworkers, who noted that if humans breathed high concentrations of  $\text{CO}_2$  for one to 2 hours, there was only a slight increment in blood bicarbonate in the face of a doubling of the arterial  $\text{CO}_2$  from 40 to 80 mm Hg and a profound drop in arterial pH (20, 196). As will be pointed out in the discussion of chronic  $\text{CO}_2$  toxicity, many hours, days, and even weeks may be required for extrarenal and renal buffer mechanisms to achieve presumably adequate total body buffering of the acidosis produced by a given level of inspired  $\text{CO}_2$ . Accordingly, it is reasonable to suggest that buffering agents be administered to compensate for this deficiency.

Very little is known about the relative contributions of an increased

partial pressure of CO<sub>2</sub> per se and the concomitant CO<sub>2</sub>-induced decrease in the pH of body tissues to the primarily neurological signs and symptoms of acute CO<sub>2</sub> toxicity (136, 155, 201, 215, 221, 225). There appears to be little doubt that CO<sub>2</sub> exerts a narcotic effect, possibly through the combination of CO<sub>2</sub> and amino acids which then participate in reversible biochemical equilibrium reactions, or through a mechanism involved in the production of general anesthesia (60, 202). On the other hand, it may well be that the manifestations of CO<sub>2</sub> toxicity are mainly due to alterations of the hydrogen ion concentration in the cellular environment. This is supported by the fact that the tolerance to high partial pressures of blood CO<sub>2</sub> of patients suffering from chronic respiratory acidosis correlates well with the ability of the body to maintain blood pH at or near normal by buffering mechanisms (136, 157, 201, 221). Westlake and coworkers (221) presented a plausible explanation for this hydrogen ion effect, noting that even small changes in intracellular pH produced by CO<sub>2</sub> will depress tissue oxygen consumption, which is a vital factor for the maintenance of consciousness. This again brings up the question of whether practical measures could be taken in an emergency situation in space to enhance the intracellular buffering capacity and so increase an astronaut's tolerance to inspired CO<sub>2</sub>.

The diuresis produced by even low toxic levels of CO<sub>2</sub> is a physiologic reaction which might conceivably have adverse effects on an astronaut. Barbour and coworkers (6) found that exposure of normal recumbent subjects to 5 and 7 percent CO<sub>2</sub> produced a threefold increase in urine output over and above the normal diuretic response to recumbency. These investigators also showed that exposure to 5 percent CO<sub>2</sub> for over 3 hours without replacing the fluid loss could lead to marked hemoconcentration. They and others have noted that the diuretic response is slight in the sitting position, may be abolished by the erect posture or by applying high tourniquets on the thighs while supine, and that it may be restored by standing in a tank of water or by mild exercise (218). Accordingly, it has been suggested but not proven that this response results from stimulation of intravascular stretch receptors in the left

atrium and pulmonary vessels by an increase in central blood volume, by some mechanical action on the atrial wall from exaggerated respiratory movements, or by an increase on the atrial transmural pressure gradient (58, 141, 218). If one or more of these mechanisms does operate to some degree, afferent connections from these receptors would inhibit the production of antidiuretic hormone by the neurohypophysis (95). Since voluntary hyperventilation, with alveolar  $\text{CO}_2$  being maintained constant by inhaling a 2 percent mixture, has been shown to produce much less of a diuresis than  $\text{CO}_2$  per se, it is also likely that  $\text{CO}_2$  acts directly on the neurohypophysis (218). Support for this action being hydrogen ion dependent is given by the findings that a  $\text{CO}_2$ -induced diuresis did not occur either when the blood pH was maintained near normal by administering a buffer on exposure to  $\text{CO}_2$ , or during the first few days at altitude when an uncompensated respiratory alkalosis would presumably have prevented the attainment of a critical intracellular pH on breathing  $\text{CO}_2$  (163, 217, 218). Finally, there still remains the possibility that  $\text{CO}_2$  might inhibit the effectiveness of antidiuretic hormone on the renal tubule (209).

Since  $\text{CO}_2$  exerts such a marked diuretic effect on man in the recumbent position, it is probable that this effect would be of similar, if not greater magnitude in the weightless environment. Study of the diuretic response to various concentrations of  $\text{CO}_2$ , especially with the exposed individual performing at various work loads, is indicated before potential hazards of such a diuresis can be implied. One would think that if a significant diuresis can occur at relatively asymptomatic levels of  $\text{CO}_2$ , exposure of an astronaut in a space suit to such levels might limit the duration of his extravehicular activity by virtue of a need to void urine. It should also be kept in mind that excess loss of body fluid will decrease tolerance to heat and cold and increase the orthostatic intolerance of an astronaut entering a gravity environment.

The effect of combined  $\text{CO}_2$  and heat stresses on man has apparently not been determined. Since they are both vasodilatory and, as previously mentioned,  $\text{CO}_2$  markedly increases sweating, it is likely that  $\text{CO}_2$  could

enhance an astronaut's susceptibility to heat disorders (Chapter 6). This could be particularly significant if an astronaut commences activity in a gravity environment after exposure to a period of weightlessness which might render him more susceptible to orthostatic intolerance.

As was pointed out in Chapter 4, CO<sub>2</sub> markedly increases an individual's susceptibility to decompression sickness. The risk of development of manifestations of decompression sickness would, of course, be enhanced still further if a CO<sub>2</sub> exposure occurs while an astronaut is performing work under conditions of decompression (Chapter 4).

A review of the literature has failed to find reference to gross or microscopic pathologic changes which can result from an acute exposure to CO<sub>2</sub>. The often marked increase in intracranial pressure, frequently accompanied by papilledema, in patients suffering from respiratory acidosis has been attributed to marked CO<sub>2</sub>-induced cerebral vasodilatation, with or without cerebral edema secondary to the altered hemostatics (136, 167). It could well be that many symptoms of acute CO<sub>2</sub> toxicity, especially those that continue for some time beyond the period of exposure, result from either cerebral edema or a vasomotor phenomenon caused by exposure to, then withdrawal from CO<sub>2</sub> environments (186). Except for these effects, which do not seem to produce permanent pathologic changes, it appears that any other temporary or permanent toxic consequences of CO<sub>2</sub> exposure would be found at the biochemical level.

#### Clinical Manifestations

The clinical manifestations of acute CO<sub>2</sub> toxicity are also well documented in the literature. Although several excellent reviews (56, 136, 155, 157, 201, 221) have discussed the consequences of acute CO<sub>2</sub> retention in patients suffering from lung disease, such information is quite impractical from the standpoint of predicting an astronaut's response to acutely elevated partial pressures of CO<sub>2</sub> in his inspired air. Caution must be taken in extrapolating to space operational situations the results

of numerous experiments in which man has been exposed from minutes to several hours to constant or gradually increasing levels of CO<sub>2</sub>. As will be pointed out in the following brief summary of these experiments, practically all CO<sub>2</sub> exposures have been carried out on resting subjects. Since exercise appears to markedly effect man's tolerance to CO<sub>2</sub>, one would not expect the results of resting exposures to be applicable to a situation in which an astronaut is exposed to elevated levels of inspired CO<sub>2</sub> while having to perform work, such as during extravehicular operations in space. It will also become apparent that past experiments have actually yielded very little information on the time of onset and the degree of functional impairment which occurred during and in the immediate period after various acute exposures to CO<sub>2</sub>. Although past experiments have yielded enough information for reasonable recommendations of maximum allowable levels of CO<sub>2</sub> for acute exposures to this gas in space, confirmatory data should be obtained in studies which simulate possible modes of exposure during operations in space, especially extravehicular activity while performing various work loads. Finally, it should be kept in mind as experimental data is taken into account, that air resistance imparted by breathing circuits could have aggravated toxic responses to CO<sub>2</sub>, and so could have produced the variable results in various studies where subjects breathed the same concentrations of CO<sub>2</sub> (8, 24, 38, 72, 160).

Much has been written on man's clinical response to various constant CO<sub>2</sub> levels to which he is acutely exposed. As pointed out above, such exposures simulate for all practical purposes the rapid increase of CO<sub>2</sub> in space suits.

Schaefer and coworkers (183, 188) recorded the symptoms experienced by 39 normal resting subjects who were alternately exposed for 15 minutes to air and, in order, 1.5, 3.3, 5.4, and 7.5 percent CO<sub>2</sub>. No symptoms were reported at the 1.5 percent level; those at other concentrations are listed in Table 15.1. It was noted that these symptoms usually appeared during the last 5 minutes of the exposures. The marked

effect which 7.5 percent  $\text{CO}_2$  had on the nervous system is readily apparent. Symptoms at this level would no doubt have led to severe impairment of performance of a psychomotor task. Also of interest was the observation that individual differences in response to  $\text{CO}_2$  in this study were related to the pre-exposure respiratory patterns of the subjects. It was noted that those individuals who had the combined respiratory characteristics of a relatively high tidal volume, slow respiratory rate and high partial pressure of alveolar  $\text{CO}_2$  before exposure to a given level of  $\text{CO}_2$ , showed less of a ventilatory response and experienced much milder symptoms than those who had the combination of a relatively low tidal volume, fast respiratory rate and low alveolar partial pressure of  $\text{CO}_2$ .

	3.3% $\text{CO}_2$	5.4% $\text{CO}_2$	7.5% $\text{CO}_2$
Dyspnea	2	4	24
Headache	0	0	15
Stomach ache	0	0	1
Dizziness	0	0	6
Sweating	1	1	5
Salivation	0	0	1
Numbness of extremities	0	0	5
Cold sensations	1	1	3
Warmth sensations	1	1	4
Increased motor activity	0	0	10
Restlessness	0	0	10
Loss of control over limbs (overactivity)	0	0	4
Loss of balance (spatial disorientation)	0	0	7
Color distortion	0	0	2
Visual distortion	0	0	6
Irritability	0	0	4
Mental disorientation	0	0	2

Table 15.1 Symptoms occurring in 39 resting subjects who inhaled  $\text{CO}_2$  for 15 minutes.

(After Schaefer et al (188)).

From numerous other studies, a more detailed  $\text{CO}_2$  response spectrum can be described. During the first day of their exposure to 3 percent  $\text{CO}_2$ , several individuals remained mentally keen in spite of exhibiting general excitement and increased activity (36, 183). Four percent  $\text{CO}_2$  was found to be the upper limit tolerated by sleeping individuals and has been shown to increase the auditory threshold significantly and to

lengthen the latent period of the negative afterimage (16, 78, 79).

Proficiency at card naming and sorting was unaltered during the exposure of 31 subjects to 5 percent  $\text{CO}_2$  for 16 minutes, although all of these subjects were moderately dyspneic, most reported fatigue, fogginess and an effort to concentrate, two experienced visual disturbances, and one failed to complete the last minute because of dizziness, marked dyspnea and impending fainting (223). It is noted that most of these individuals, of whom many were experienced pilots, were of the opinion that 5 percent  $\text{CO}_2$  for a 16 minute period was close to a marginal concentration for the safe operation of an automobile or airplane (225). Other studies carried out at the 5 percent level have found a significant increase in the pain threshold and decrease in the fusion frequency of flicker (189, 204, 209).

Two observers who entered a 5.7 percent  $\text{CO}_2$  atmosphere in which several individuals were tolerating a gradual increase of  $\text{CO}_2$  immediately became so dyspneic that they were unable to make observations (28). Seven subjects tolerated 6 percent  $\text{CO}_2$  for about 22 minutes, but experienced marked dyspnea, flushing and sweating of the face, and feelings of stupification and impending collapse, especially toward the end of the exposure (29). Visual intensity discrimination has also been shown to be affected in studies at the 6 percent level (74). Prolongation of the time required for addition and cancellation tests, and the existence of dissociation, perseveration and an increase in the unusualness of response has been demonstrated in subjects breathing 6 to 7 percent  $\text{CO}_2$  (76, 77).

In contrast to the symptoms reported in the above exposures to 6 percent  $\text{CO}_2$ , the "mental status seemed unaffected" in 7 subjects who breathed 7 percent  $\text{CO}_2$  for 40 to 90 minutes, although all suffered from dyspnea and some complained of mild headache and burning of the eyes (20). Exposure to 7.5 percent  $\text{CO}_2$  for 3.5 to 6 minutes has been tolerated, but symptoms had a shorter lag time than in 7 percent  $\text{CO}_2$  (29). The 7.5 percent  $\text{CO}_2$  level has also been found to decrease the inhibitory effect of light stimulation on brain waves - a finding which demonstrated the depressive or narcotic action of  $\text{CO}_2$  on the central nervous system (189). An experiment in which 42 subjects who breathed 7.6 percent  $\text{CO}_2$  for

2.5 to 10 minutes yielded results similar to the other experiments near this CO<sub>2</sub> level, although one subject did lose consciousness (29, 188).

Individuals who have been exposed to 10 percent CO<sub>2</sub> have immediately experienced one or more of a number of clinical manifestations, such as extreme dyspnea, visual and auditory hallucinations, chilliness, nausea, and vomiting, a strangling sensation, burning of the eyes, cloudiness of vision and profuse sweating. They have usually become stuporous within 10 minutes and lose consciousness within 15 minutes (29, 41, 55, 64, 199, 222). Although CO<sub>2</sub> concentrations of over 20 percent have been used for the treatment of mental disorders and experimentally for anesthesia, it is considered probable that if an individual who does not have the benefit of therapeutic support is exposed to CO<sub>2</sub> levels above 10 percent, he will rapidly suffer the sequence of respiratory depression, convulsions, "shock", and death (116, 132, 135, 222).

The classic work of Haldane and Smith in 1892 (90) elicited many of the clinical manifestations to be expected from exposure to gradually increasing inspired CO<sub>2</sub>. These investigators had normal resting subjects rebreathe air while enclosed in a 70 cubic foot chamber. As noted previously, the rate of CO<sub>2</sub> accumulation in this volume would apply to that generally expected in spacecraft cabin atmospheres. In one experiment, chamber CO<sub>2</sub> increased linearly over an 8 hour period to 6.4 percent, while oxygen decreased to 13 percent. About 4 percent CO<sub>2</sub>, the subject became aware of increased breathing and began to complain of headache and nausea. For the last two hours of exposure, when CO<sub>2</sub> had passed about 5.2 percent, breathing was "painfully labored and required so much exertion as to cause great exhaustion". This marked dyspnea eventually caused termination of the experiment. Another subject showed a similar response, having to end his 7 hours in the chamber after linear CO<sub>2</sub> and oxygen changes to 5.8 and about 14 percent, respectively. By allowing changes in either CO<sub>2</sub> or oxygen in the chamber, Haldane and Smith (90) showed that the decrease in inspired oxygen in the above experiments could not have been a factor in producing these various manifestations of rebreathing air until the oxygen concentration fell below



13 percent. Finally, they demonstrated that resting subjects who re-breathed air from a 225 liter bag could tolerate a maximum  $\text{CO}_2$  concentration of about 10 percent, attained in about 1.5 hours. They suffered from mental confusion and extreme perspiration in addition to the manifestations described above, as this level was reached.

Studies by Brown in 1930 (28, 29) have also yielded valuable information on man's response to gradually increasing inspired  $\text{CO}_2$ . Normal resting subjects in groups of four rebreathed 654 cubic feet of chamber air (164 cubic feet per man). In the first experiment described, the chamber  $\text{CO}_2$  increased linearly to 4.7 percent, while oxygen decreased to 15.5 percent, over a period of 10 hours. At about 2 percent  $\text{CO}_2$ , "active exertion had an effect on respiration". All subjects tolerated this exposure, none complaining of actual dyspnea; one suffered from a mild headache for the last 3 hours. General fatigue and listlessness experienced during the exposure did not seem to alter subject alertness. In the second experiment,  $\text{CO}_2$  was gradually introduced into the chamber, with linear changes in this gas and oxygen to 4.8 and 17.8 percent, respectively, taking about 5.3 hours. Notably, all subjects reported chilly sensations during the final hours, in spite of an average chamber temperature of 75° F and relative humidity of 74 percent. Oral temperatures recorded in three subjects fell 1.0, 2.2, and 3° F. Again, dyspnea was noted, mild headache occurred in one subject, and general fatigue and listlessness were outstanding. In the third experiment,  $\text{CO}_2$  was again introduced into the chamber, and changed along with oxygen in an essentially linear manner until these gases reached 5.2 and 15.6 percent, respectively, by the end of 8 hours. Breathing became decidedly labored for all subjects, with two reporting dyspnea in the last half hour, when the  $\text{CO}_2$  level was above about 4.8 percent. Fatigue was more marked than in the above experiments and again all subjects had chilly sensations, associated with a fall in body temperature. Three experiments similar to the last reached 5.6, 5.7, and 5.8 percent  $\text{CO}_2$  and 16.1, 15.4, and 14.2 percent oxygen in 8 hours. All subjects made note of experiencing a pronounced increase in the depth of breathing soon after the 4 percent  $\text{CO}_2$  level was reached, the

stage of panting virtually setting in at this time. During the last hour in all three of these experiments, when  $\text{CO}_2$  was above 5.1 percent, all subjects except one who was found to be relatively resistant to  $\text{CO}_2$ , complained of dyspnea in addition to exhaustion from severe panting. Most reported headache, which was frequently associated with nausea, for the last two hours, when the  $\text{CO}_2$  was above 4.6 percent. Again, mild hypothermia with associated chilly sensations occurred in spite of the subjects being in a presumably comfortable environment. A number of experiments with similar increases of  $\text{CO}_2$  as those above, but with oxygen maintained near normal levels, ruled out a significant contribution of decreased oxygen, at least down to the 15.5 percent level, in producing these various toxic manifestations. From his own and other past studies, Brown estimated that oxygen depletion would begin to have an effect about the 14 percent level. In the experiments where  $\text{CO}_2$  and oxygen reached respective levels of 5.8 and 14.2 percent, and 5.3 and 20.5 percent, Brown found evidence that excellent psychological reserve was maintained, with subjects failing to show an altered response to a variety of tests of attention, memory, association, deduction, and motor coordination.

Other studies have substantiated the findings of Haldane and Smith, and Brown (1, 42, 89, 92, 98, 194). In experiments in which inspired  $\text{CO}_2$  increased to the 5 to 7 percent range in one to 4 hours, it was also noted that the incidence of clinical manifestations of  $\text{CO}_2$  toxicity increased rapidly above 5 percent  $\text{CO}_2$  <sup>(92)</sup>. Particular attention is drawn to the occurrence of nausea and vomiting above this level, for vomiting in the weightless environment will be an extremely hazardous event (Chapter 8) <sup>(192)</sup>. Mental confusion and dizziness occurred about 7 percent  $\text{CO}_2$  <sup>(92)</sup>. In other rebreathing experiments, the maximum tolerable limit was again about 10 percent  $\text{CO}_2$ , this level being reached in about 4 hours <sup>(98)</sup>.

As mentioned above, symptoms can be experienced after the cessation of certain exposures to  $\text{CO}_2$  and, as the examples given below will show, can result in even greater functional impairment than symptoms experienced

during such exposures. This phenomenon may have been a major factor preventing the successful escape of personnel from the sunken submarine Thetis <sup>(1)</sup>.

A number of CO<sub>2</sub>-withdrawal symptoms have been reported following exposures to various maintained levels of CO<sub>2</sub>. This reaction and its marked variability was well demonstrated by a study in which 5 subjects breathed 6.7 percent CO<sub>2</sub> for one hour <sup>(1)</sup>. On ceasing their exposure, one subject immediately vomited repeatedly and complained of nausea and headache, two experienced temporary severe incapacitating headaches, and two complained of only slight headache. In other studies, subjects exposed to 3 percent CO<sub>2</sub> for many hours apparently complained of only a mild headache on returning to air <sup>(36, 179)</sup>. Headache was also complained of after exposures to 5.2 and 6.4 percent CO<sub>2</sub> for 2 hours <sup>(50)</sup>. A frequent symptom after cessation of exposures to 7.6 percent CO<sub>2</sub> for an average of 7.4 minutes and 10.4 percent CO<sub>2</sub> for an average of 3.8 minutes was temporary dizziness <sup>(55)</sup>.

Clinical manifestations have also occurred after withdrawal from exposure to gradually increasing ambient CO<sub>2</sub> levels. A classical example of a particularly severe CO<sub>2</sub>-withdrawal reaction was cited by Alexander and coworkers <sup>(1)</sup>. Their subject tolerated an increase in CO<sub>2</sub> to 6.6 percent over a 14.5 hour period, yet, when subsequently exposed to oxygen, immediately vomited a pint of clear fluid in spite of not having ingested anything for over 16 hours. He also began to suffer immediately from a violent diffuse headache, which appears to have incapacitated him for about an hour. In the Haldane and Smith study <sup>(90)</sup> the headache and nausea experienced by the two subjects, as CO<sub>2</sub> increased to 6.4 and 5.8 percent over 7 and 8 hours, was reported to have temporarily worsened when they left the chamber. In Brown's experiments <sup>(28, 29)</sup>, withdrawal from concentrations of CO<sub>2</sub> reaching from 4.8 to 5.8 percent over 5.3 to 10 hours was accompanied either by the onset or aggravation of headache or nausea which lasted for 1 to 3 hours. Hayter and Duffner <sup>(92)</sup> found that for an as yet unexplained reason, the headaches resulting from exposure to CO<sub>2</sub>, which increased to 5 to 7 percent over one to 3 hours, were much worse, occurred with

greater frequency, and lasted much longer in subjects who breathed air as compared to those who breathed oxygen after exposure.

The cause of the above clinical manifestations of CO<sub>2</sub> withdrawal is unknown. The brief hypotension which coincided with the temporary dizziness immediately after ceasing the brief exposures to 7.6 and 10.4 percent CO<sub>2</sub> might possibly be due to the vasodilatory action of CO<sub>2</sub> persisting beyond its sympathetic action in the immediate post-exposure period (55, 167). Other effects of altered sympatho-adrenal activity, which could accompany CO<sub>2</sub> withdrawal, might conceivably cause symptoms (141). Whether the temporary undershoot of alveolar CO<sub>2</sub>, observed when 15 minute exposures to 5.4 and 7.5 percent CO<sub>2</sub> were terminated, might produce a hypocapnia of a sufficient magnitude to produce a symptom such as dizziness remains to be determined (188). Finally, it is conceivable that a cerebral vasomotor phenomenon caused by exposure to, then withdrawal from a CO<sub>2</sub> environment might be a major etiologic factor (186).

A review of the pertinent literature indicates it is unlikely that CO<sub>2</sub> exposures in space will ever be severe enough to cause such serious consequences of CO<sub>2</sub> withdrawal as prolonged profound hypotension and grave cardiac arrhythmias which are prone to occur following marked CO<sub>2</sub> retention in anesthetized patients (25, 26, 31, 39, 83, 137, 155, 166, 167).

Finally, it is pointed out that certain symptoms which are not really specific effects of CO<sub>2</sub> withdrawal might occur in the post-exposure period. Marked, general fatigue, and soreness in the region of the diaphragm have been reported after most of the prolonged acute exposures to over 4 percent CO<sub>2</sub> described above. Such symptoms could no doubt limit an astronaut's physical work capacity for several hours after such an exposure. Conceivably, intense shivering might be experienced after certain exposures to CO<sub>2</sub> which, as mentioned above, can cause an excessive loss of body heat during exposure.

The results of most of the experiments in acute CO<sub>2</sub> toxicity have been summarized graphically in Figure 15.3 for CO<sub>2</sub> exposures of up to

80 minutes. This graph again points out that resting man appears to tolerate acute exposures to about 3 per cent  $\text{CO}_2$  quite well. It should also be noted that the degree of distracting discomfort between 3 and 4 percent  $\text{CO}_2$  is minimal, and beyond 4 percent symptoms rapidly appear and become functionally limiting.

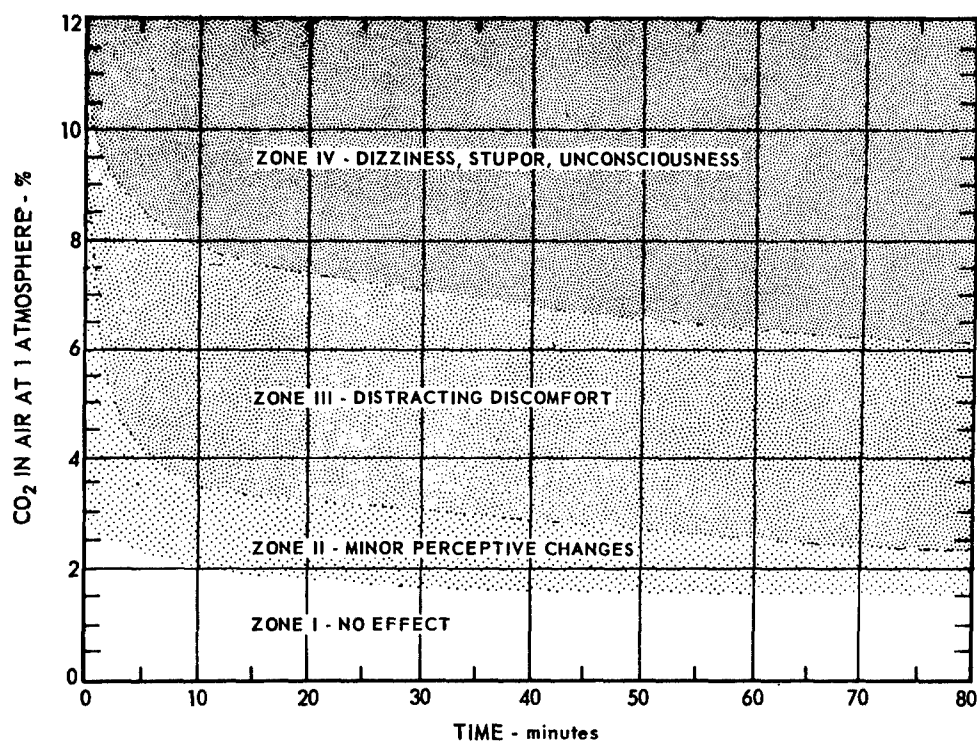


Figure 15.3 General symptoms experienced by most resting subjects when exposed for the times indicated to mixtures of carbon dioxide in air at a total pressure of one atmosphere.

(Drawn from data of King (103), Nevison (150) and Schaefer (180) for Bioastronautics Data Book (149)).

This graph also points out the fact that relatively high concentrations of  $\text{CO}_2$  can be tolerated by resting man for only brief periods of time. Accordingly, it would not be wise to recommend short-time maximum allowable limits for emergency situations in space, especially for extra-vehicular operations when performing quite high work loads.

It is apparent both from foregoing discussions and this graph that man can better tolerate an acute exposure to  $\text{CO}_2$  which accumulates in his

atmosphere slowly rather than rapidly. However, the gain in tolerance to CO<sub>2</sub> by allowing this gas to accumulate slowly tends to be nullified by the subsequent consequences of CO<sub>2</sub> withdrawal. It is again emphasized that an extremely serious situation could develop in an astronaut, who has tolerated a gradual increase in his inspired CO<sub>2</sub>, should vomit into his weightless environment or suffer from a functionally incapacitating headache as the result of CO<sub>2</sub> withdrawal.

### Diagnosis

Acute CO<sub>2</sub> toxicity should usually be easily recognized in space, for an astronaut should know of a partial or complete failure of his CO<sub>2</sub>-absorbing system for minutes to hours prior to experiencing symptoms. A possible exception to this could be temporary overloading of a CO<sub>2</sub>-absorber, especially that of the space suit. Accordingly, it is considered most important to have devices which monitor closely vital environmental control system functions and the partial pressure of CO<sub>2</sub> at appropriate sites in the extravehicular life support system or space suit helmet, and in the spacecraft cabin. Such a monitoring system should also provide an adequate signal to an exposed astronaut and other members of the crew if a system begins to malfunction or CO<sub>2</sub> accumulation occurs. The many clinical manifestations which point diagnostically to acute CO<sub>2</sub> toxicity are apparent from previous discussion.

### Prevention

As subsequent discussion will point out, there is at present no practical measure for the specific treatment of acute CO<sub>2</sub> toxicity in space. Therefore various modes of keeping an astronaut's partial pressure of inspired CO<sub>2</sub> below reasonably safe levels might have to be completely relied upon during operations in space. Environmental control systems must be designed to handle immediately all possible peak CO<sub>2</sub> loads. The reliability of these systems can be increased with emergency subsystems which either absorb CO<sub>2</sub> or purge atmospheres of the gas. An astronaut might be supplied his breathing gas directly by mask or

mouthpiece if exposed to a toxic ambient CO<sub>2</sub> level. Finally, activation of one or more extravehicular life support systems might suffice temporarily for CO<sub>2</sub> removal from a spacecraft cabin atmosphere.

In the light of previously mentioned factors which must be taken into account when recommending maximum allowable, "acute" levels of CO<sub>2</sub> for space atmospheres, data on past exposures of man to CO<sub>2</sub> indicate that:

- the CO<sub>2</sub> level in the spacecraft cabin should never exceed 3 percent, or a partial pressure of 22.5 mm Hg., for more than several hours in duration. In stating this level, it is assumed that the astronaut will be awake and performing only light work during his exposure. Although symptoms such as a noticeable increase in breathing and, following longer exposures, a mild headache can be expected during exposure and for some time after exposure to this level, they should not significantly affect an astronaut's functional capacity.

- the CO<sub>2</sub> level in the space suit helmet should never exceed 2 percent, or a partial pressure of 15 mm Hg. In stating this level, it is assumed that the astronaut will always be moving about or working in his pressurized suit, and so performing up to a very high work load during his exposure. Dyspnea can be expected at this level of CO<sub>2</sub>, particularly at moderate or high work loads. However, if the astronaut controls his work load and allows time for excess CO<sub>2</sub> to be purged and possibly absorbed from his space suit atmosphere, he should be able to keep this symptom from becoming severe enough to prevent his executing a required task before he returns to the spacecraft.

- space suit environmental control systems should be designed to maintain space suit helmet CO<sub>2</sub> always below one percent or 7.5 mm Hg. This would allow for some CO<sub>2</sub> accumulation and yet have the level of inspired CO<sub>2</sub> kept well below that which could adversely affect the astronaut, especially when he has to perform at high work loads.

### Treatment

The question has already arisen as to whether there is a practical measure which might be used in space to increase an astronaut's tolerance to acutely elevated inspired CO<sub>2</sub>. Looking back over the literature, it is

found that during World War II, Pointer <sup>(164)</sup> attempted to find a way of increasing the CO<sub>2</sub> tolerance of submarine personnel by having these individuals ingest rather large amounts of sodium and potassium salts while exposed to a 2 to 3.5 percent CO<sub>2</sub> atmosphere. These alkaline salts did shorten the time for blood pH to return to normal, and treated individuals suffered somewhat less from symptoms of acute CO<sub>2</sub> toxicity, such as headache and restlessness, as compared to those untreated. However, the value of this medication was not permanent, as the degree of affected performance, as will be described under "Chronic CO<sub>2</sub> Toxicity", was similar in both groups when their CO<sub>2</sub>-induced acidosis was apparently totally buffered, or compensated for by body buffer mechanisms. As to whether such a measure could be used for the treatment of acute CO<sub>2</sub> toxicity in space is debatable, for it is thought that the rate and degree of enhanced body buffering which could be attained with these salts would fail to compensate adequately for either the rapid rises or the high levels of CO<sub>2</sub> which could be reached during space operations. Also militating against the use of these salts in space is the tendency for large doses to produce irritation of the gastrointestinal tract.

More recently, other measures have been utilized in attempts to combat body pH changes, and so improve the state of patients suffering from acute CO<sub>2</sub> retention, or uncompensated respiratory acidosis due to lung disease. Results with infusions of sodium lactate and sodium bicarbonate have not been encouraging, for only weak alkaline solutions can be tolerated intravenously, thus necessitating the administration of large volumes of fluid over a prolonged period of time to give any sustained effect <sup>(128, 186, 202)</sup>. Moreover, these solutions are not really suitable for the treatment of hypercapnia since they generate CO<sub>2</sub> and, therefore, increase the amount of CO<sub>2</sub> which has to be excreted by the lungs <sup>(141)</sup>.

In 1959, Nahas <sup>(139)</sup>, noting that organic CO<sub>2</sub> buffers were highly capable of maintaining virtually constant partial pressure of CO<sub>2</sub> in the gas phase of in vitro systems, suggested that such buffers, in parti-



cular tris (hydroxymethyl)-aminomethane\*, or so-called tris buffer, might be found useful in treating respiratory acidosis (108, 159).

Tris buffer rapidly distributes itself throughout both the intra- and extracellular spaces (140). It exerts a large part of its titrating effect in the extracellular compartment by increasing the buffer capacity of this compartment, which acts as a CO<sub>2</sub> "sink" (141). By decreasing the partial pressure of CO<sub>2</sub> in the extracellular fluid, tris buffer also decreases the partial pressure of CO<sub>2</sub> in the intracellular compartment, with a resulting increase in pH therein (140). It is also true that this agent penetrates the intracellular compartment to some degree, but its intracellular titrating effect should not be quantitatively as important as its extracellular titrating effect (141).

Numerous investigators have assessed the therapeutic effectiveness of tris buffer in various studies in animals and humans (12, 14, 21, 22, 23, 27, 59, 101, 117, 122, 128, 139, 142, 144, 146, 154, 202).

However, reports indicate that results of treating patients in uncompensated respiratory acidosis with tris buffer have not been startling and, therefore, do not support the use of this drug in an emergency situation in space (21, 122, 128, 154, 202). Tris buffer has been difficult to use and has produced a number of serious side-effects. Taken orally, it is unpalatable and usually produces severe diarrhea (22). Notably, weak acid salts of tris buffer, which retain up to 70 percent of their titrating activity, were administered orally in one study to animals for periods of up to 3 months (148). Gastrointestinal disturbances were apparently not observed in these animals. The base content of the blood remained significantly elevated during the period of administration. This raises the question as to whether or not there is indeed a conjugated form of tris buffer that can be tolerated when taken orally by man. If so, it is thought that short periods of CO<sub>2</sub> inhalation might be better tolerated by individuals in whom the buffering capacity of the body fluids has been elevated by this agent (141). Intensive experimentation is warranted

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\* Tris (hydroxymethyl)-aminomethane works according to the general equation  
$$\text{R-NH}_2 + \text{H}_2\text{O} + \text{CO}_2 \rightleftharpoons \text{HCO}_3^- + \text{RNH}_3^+$$

to assess practicability of this measure.

Tris buffer has been routinely administered intravenously to patients. Even then, severe vascular irritation and thrombosis, and sloughing of tissue due to extravasation of this agent at the site of infusion have occurred all too frequently (21, 22). Studies in which the acidosis of individuals acutely exposed to elevated levels of inspired  $\text{CO}_2$  was corrected with tris buffer have shown that because of its rapid short-term action, this agent must be administered continuously, preferably with the blood pH being monitored. While changes in blood pH due to  $\text{CO}_2$  are being adequately controlled with tris buffer, sudden and drastic changes in the body's electrolyte balance and a marked hypoglycemia, even if glucose is given in the infused solution, can occur (27, 154). Electrolyte loss is probably the cause of the prolonged retching, weakness and somnolence observed after such infusions (27). Finally, it is important to point out that tris buffer appears to produce a profound respiratory depression, apparently due to intracellular hydrogen ion buffering in the respiratory centers. Administration of this agent to animals and normal individuals who are not exposed to elevated levels of inspired  $\text{CO}_2$ , to normal individuals who are exposed to elevated levels of inspired  $\text{CO}_2$ , and to patients suffering from acute  $\text{CO}_2$  retention or uncompensated respiratory acidosis due to lung disease has produced concomitant decreases in the arterial oxygen tension (14, 22, 23, 27, 122, 142, 154, 202). This side-effect might also contraindicate the use of tris buffer in space, especially in a borderline hypoxic situation.

From the above discussion, it is apparent that there is at present no specific practical measure which might be used to combat the toxic effects of  $\text{CO}_2$  on an astronaut. Since the acidosis accompanying acute  $\text{CO}_2$  toxicity corrects itself within a few minutes, after even a prolonged acute  $\text{CO}_2$  exposure, it is important to remember that the administration of a buffering agent to an astronaut who has suffered a severe exposure would not be effective (216). More important, however, would be to assure him adequate ventilation and to treat the consequence of possible associated hypoxia (Chapter 1). Whether various drugs in common use might be effective in treating symptoms of  $\text{CO}_2$  toxicity,

such as headache, nausea, and vomiting remains to be determined, for a therapeutic attack on symptoms in either the exposure or post-exposure period has apparently not been attempted during past exposures of man to acutely elevated inspired levels of CO<sub>2</sub>.

### Chronic CO<sub>2</sub> Toxicity

The above heading encompasses a possible exposure of an astronaut to a toxic partial pressure of CO<sub>2</sub>, this exposure lasting for days to weeks and even many months in duration. Two possible causes for such an exposure, which can lead to a spectrum of clinical manifestations quite different to that of acute CO<sub>2</sub> toxicity, are conceivable. Firstly, a spacecraft life support system could malfunction for a prolonged period of time, possibly until the completion of a mission. Secondly, it is considered possible that the upper limit of atmospheric CO<sub>2</sub> specified for a normally operating spacecraft life support system might be too high, the decision for this limit being implied from ground-based studies which have been too short in duration to have elicited clinical manifestations. As well, it has been stated that a somewhat elevated partial pressure of CO<sub>2</sub> in space atmospheres would not only increase the efficiency of physical, chemical and biotic CO<sub>2</sub> scrubbers but, as a consequence, enable reductions of such highly significant penalties imposed by a life support system as weight, volume, and power (7, 47, 94).

As will become readily apparent in the following discussion, the maximum allowable levels of CO<sub>2</sub> for chronic exposures in space and the possible medical problems resulting from chronic exposures above these levels will have to be determined from a very few studies in which man has been exposed to relatively low CO<sub>2</sub> levels for prolonged periods of time. In fact, the longest of all such exposures lasted for only 6 weeks. Therefore, it will be most important to have a critical look at even minor physiological changes which have occurred during these exposures, being careful not to assume that the absence of clinical manifestations of CO<sub>2</sub> toxicity in them would necessarily also

hold for longer exposures during prolonged space missions.

### Pathophysiology

"Operation Hideout", a study in which 23 normal subjects were exposed to 1.5 percent  $\text{CO}_2$  in air for a period of 42 days, has yielded the greatest amount of data to date on the physiological and possible pathological effects on man from a prolonged exposure to a relatively low level of  $\text{CO}_2$ . Averaged results of this study, which have been discussed in numerous publications by Schaefer and coworkers (18, 105, 180, 181, 182, 184, 185, 191, 192, 193), indicated that no alterations in basic physiologic parameters, such as blood pressure, pulse rate, weight and temperature, occurred. On the other hand, data on respiration, acid-base balance, calcium and inorganic phosphorus metabolism, adrenal cortical activity, and cardiovascular capacity revealed significant changes, some of which might have important clinical implications. Before presenting the data considered pertinent to assessing potential harmful effect of 1.5 percent  $\text{CO}_2$  on man, it is noted that even though most of the changes occurring in this study continued throughout the 9 day post-exposure study period, all had essentially returned to pre-exposure levels after 4 weeks of breathing air.

Alterations of blood and urine pH, and urine  $\text{CO}_2$  clearly indicated the existence of a phase of slight uncompensated respiratory acidosis for the first 23 days, followed by a phase of compensated respiratory acidosis for the remainder of the exposure. In spite of the increase in respiratory minute volume in response to 1.5 percent  $\text{CO}_2$  during these phases, the partial pressure of alveolar  $\text{CO}_2$  still rose about 3 mm Hg throughout the exposure and the 9 day post-exposure study period. This ventilatory effect was the net result of a progressive increase in tidal volume and decrease in respiratory rate during exposure, with a further drop in respiratory rate and slight rise in alveolar  $\text{CO}_2$  occurring when air was again breathed. A diminished respiratory responsiveness to 5 percent  $\text{CO}_2$  was demonstrated when the acidosis was compensated, presumably due to the increase of the buffering capacity of the body secondary to the breathing of  $\text{CO}_2$ . Whether such

an alteration in buffering capacity would significantly alter an astronaut's clinical response to an acute CO<sub>2</sub> exposure cannot be determined from this data.

Possibly relevant to assessing whether or not 1.5 percent CO<sub>2</sub> can be significantly toxic for man was the finding that all respiratory dead spaces, and both arterial alveolar CO<sub>2</sub> and oxygen gradients were elevated during the exposure, especially in the uncompensated phase of respiratory acidosis and during the 9 day post-exposure study period. Although it was pointed out that such dead space and gradient changes might be explained on the basis of the increased tidal volume, possible airway dilatation and possible altered pulmonary perfusion from breathing CO<sub>2</sub>, the thought that actual physicochemical and even pathologic changes in the subjects' lungs might have contributed was also entertained (191). Microscopic studies of the lungs of animals chronically exposed to low ambient CO<sub>2</sub> levels have found evidence suggesting that such an exposure alters production of pulmonary surfactant, and leads to atelectasis, hyaline membrane formation and perivascular edema (12, 133, 153, 187). Because these harmful effects of CO<sub>2</sub> on animals' lungs were apparently seen only during the uncompensated phase of respiratory acidosis, they were attributed to the acidosis rather than to a direct action of CO<sub>2</sub>. Whether such effects could occur to a significant degree in man, possibly increasing the susceptibility of his lungs to secondary infection, to damage by elevated partial pressures of oxygen, or to atelectasis in pure oxygen atmospheres remains to be determined.

Blood and urine pH, and total pulmonary and urinary CO<sub>2</sub> excretion were reduced below control values during the 23 day period of uncompensated respiratory acidosis. During the phase of compensated respiratory acidosis, the blood pH returned to control values, whereas the urinary and pulmonary CO<sub>2</sub> excretion and the urine pH were elevated above control values. After transition to air, CO<sub>2</sub> stored by the body during the exposure appeared to be almost entirely eliminated in 9 days. In the post-exposure period, the increased pulmonary CO<sub>2</sub> excretion peaked on the first and eighth days and the increased urinary CO<sub>2</sub> excretion, paralleled by the elevated urine pH, peaked on the second day. Accordingly,

it was suggested that this release of  $\text{CO}_2$  occurred at different rates from three different body  $\text{CO}_2$  stores (185, 192).

Studies of calcium and inorganic phosphorus metabolism brought to light the mechanisms apparently responsible for the pH and  $\text{CO}_2$  changes noted above. The venous plasma ionized calcium paralleled the changes in blood pH, showing a decrease during the first 23 days of exposure, a return to normal levels during the latter part of the exposure, and a rise above control values during the 9 day post-exposure study period. This suggested that the long time period for  $\text{CO}_2$  retention, or the phase of uncompensated respiratory acidosis, was related to the slow equilibration of the bone  $\text{CO}_2$  store with the elevated blood  $\text{CO}_2$ . Furthermore, a blood calcium tide, commensurate with the highest peak in pulmonary  $\text{CO}_2$  excretion and an increased urinary calcium excretion, occurred 8 days after ceasing the exposure to  $\text{CO}_2$ . This seemed to indicate that at this time, the bones released much of their previously stored  $\text{CO}_2$ . The plasma inorganic phosphorus was elevated throughout the exposure period, and apparently up to 4 weeks post-exposure. The urinary inorganic phosphorus excretion increased markedly during the phase of uncompensated respiratory acidosis and, except for a transient sudden fall 8 days post-exposure, remained so for the rest of the exposure and post-exposure study periods.

In the detailed discussion of urinary calculus formation in Chapter 9, it was pointed out that increased urine pH and calcium levels, especially if occurring together, are factors conducive to urinary calculus formation. Since the urine pH was elevated above control values during the phase of compensated respiratory acidosis, and both the urine pH and calcium were elevated above control values in the 9 day post-exposure study period, it is conceivable that a chronic exposure to  $\text{CO}_2$  could be associated with a risk of a calculus forming and growing in the urinary tract. If so, repeated chronic exposures would increase the likelihood of a calculus reaching such a size as to cause symptoms. Evidence which seems to support this hypothesis is found in animal experiments in which chronic exposures to relatively low levels of  $\text{CO}_2$  resulted in the deposition of calcium in, and associated damage of kidney

tissues (133, 186, 190, 206). On the other hand, the literature has not recorded any increased incidence of urinary tract problems in submarine crews who have been repeatedly subjected over several days or weeks to ambient CO<sub>2</sub> levels which often reached up to 3.5 percent. In fact, the only pathology apparently associated with altered calcium metabolism in these crews has been the presence of areas of hypercalcification in the fingernails (164). Even though an epidemiological study may prove that there is no significant risk of urinary calculus in individuals chronically exposed to CO<sub>2</sub> on Earth, it is still considered possible that this risk might become significant in space if urine changes due to CO<sub>2</sub> were combined with those resulting from perhaps even a minor degree of bone demineralization due to reduced physical activity and weightlessness.

What might well be a significant effect of CO<sub>2</sub> on man is the increase in adrenal cortical activity which was found during the 42 days of exposure to 1.5 percent CO<sub>2</sub> and the 9 day post-exposure study period (104). This response, mirrored by an increase in the ketosteroid output in the urine and a decrease in the absolute number of circulating eosinophils, was greater during the phase of compensated respiratory acidosis and post-exposure study period than early in the phase of uncompensated respiratory acidosis. It was also noted that the number of complaints showed a trend opposite to changes in adrenal cortical activity (107). Accordingly, Schaefer (180) has suggested that independent of blood pH changes, an increase of the partial pressure of CO<sub>2</sub> in the blood might produce a significant "physiologic stress" response. This suggestion appears to be supported, not only by identical findings as those stated above, but also by histologic evidence of adrenal cortical strain in a study in which rats and guinea pigs were exposed to 1.5 percent CO<sub>2</sub> for 42 days (106). However, it would appear that the possibility "physiologic stress" due to confinement and handling of the exposed animals was not ruled out by having unexposed control animal groups in these studies (70). It is also noted that in human studies, confinement per se produces an adrenal cortical response similar to that observed in "Operation Hideout" (71). The importance of having control groups in

future animal and human chronic CO<sub>2</sub> studies cannot be overemphasized. If CO<sub>2</sub> is found to produce changes in adrenal function, one wonders whether a chronic exposure to a relatively low level of CO<sub>2</sub> could significantly alter the body's capacity to handle such superimposed stresses as infection, hemorrhage, plasma loss, acute radiation effects and severe tissue trauma. This certainly appears to be an area requiring investigation.

Finally, it should be mentioned that the cardiovascular capacity, as measured by various tests of cardiovascular function when the subjects were subjected to various work loads, decreased significantly throughout the exposure to 1.5 percent CO<sub>2</sub> and during the 9 day post-exposure study period. Although the subjects were undoubtedly carrying out less physical activity during the period of confinement, this reduction of circulatory reserve has been attributed mainly to CO<sub>2</sub> (185). Again, the importance of control studies bears re-emphasizing. If this level of CO<sub>2</sub> does affect cardiovascular function, the question arises as to what effect it might have on the performance of various work loads.

Man's response to 3 percent CO<sub>2</sub> has been observed in chronic exposures of a much shorter duration than that of "Operation Hideout". Schaefer (176, 177) exposed subjects to 3 percent CO<sub>2</sub> in air for periods of up to 144 hours. He found that the phase of uncompensated respiratory acidosis lasted only 2 to 3 days, indicating that renal mechanisms rather than bone CO<sub>2</sub> stores were primarily responsible for the return of blood pH to normal values (185). Various recorded physiologic changes and alterations in subjective complaints and performance to be discussed, indicated that the phases of uncompensated and compensated respiratory acidosis were associated with respective increases of sympathetic and parasympathetic nervous system tone. Increased sympathetic tone was characterized by significant increases above control values of resting pulse rate, neuromuscular excitability, responsiveness of the circulatory system to exercise and heat production after a cold load. The most undesirable clinical manifestations from breathing 3 percent



CO<sub>2</sub> appeared during the phase of increased parasympathetic tone, which was characterized by significant decreases of these physiologic parameters to below control values. Schaefer <sup>(179)</sup> noted that this phase continued for about 5 days into the post-exposure study period and could be maintained if subjects extended their exposure to 3 percent CO<sub>2</sub>, but breathed this gas for only 8 hours daily. Finally, he substantiated the findings in this study with observations made during chronic exposures of submarine crews to CO<sub>2</sub> levels in the range of 3 percent, pointing out that the concomitant lowering of the level of oxygen in the submarine atmospheres would not have been sufficient enough to have played a significant role in causing the effects noted above.

Another study with 3 percent CO<sub>2</sub> has more closely simulated possible chronic exposures to CO<sub>2</sub> in low pressure, oxygen enriched, space atmospheres <sup>(47)</sup>. Eight normal individuals successively breathed, for periods of 4 days, atmospheres of air at 700 mm Hg; air at 700 mm Hg, containing CO<sub>2</sub> at 21 mm Hg; air at about 747 mm Hg; oxygen at 200 mm Hg; and oxygen at 200 mm Hg, containing CO<sub>2</sub> at 21 mm Hg. There was no difference in either the ventilatory response to CO<sub>2</sub> or the increase of the partial pressure of alveolar CO<sub>2</sub> produced by breathing CO<sub>2</sub> at these different ambient atmospheric pressures. The respiratory acidosis, as noted by changes in blood pH was essentially compensated in 3 days in each CO<sub>2</sub> exposure period. This blood pH change has also been observed in a recent study in which normal individuals breathed air at 700 mm Hg, containing CO<sub>2</sub> at 21 mm Hg for 5 days <sup>(80)</sup>. Finally, it is noted that these and other recorded physiologic parameters studied demonstrated that the partial pressure of inspired oxygen being the same, the response of man to CO<sub>2</sub> in a low pressure atmosphere is essentially the same as for an equivalent partial pressure of CO<sub>2</sub> at an atmospheric pressure near sea level.

In yet another study at the 3 percent CO<sub>2</sub> level, respiratory center sensitivity of 2 normal individuals who breathed this level for 78 hours decreased significantly <sup>(36)</sup>. This was indicated by an increase in the breath-hold break-point, a decrease in the ventilatory response to

a CO<sub>2</sub> load, and a temporary, further increase in alveolar CO<sub>2</sub> on breathing air at the end of the exposure. Similar findings have been reported elsewhere in this chapter and in the literature (176, 179). As pointed out above, the question as to whether a chronic, compensated exposure to CO<sub>2</sub> could significantly alter an astronaut's physiological, and hence clinical tolerance to an acute CO<sub>2</sub> exposure remains to be answered.

The marked predisposition of patients suffering from emphysema and other hypoventilatory states to develop peptic ulceration has been well documented (87, 115, 151, 162, 172, 203). One wonders, therefore, whether an astronaut who is chronically exposed to an elevated level of inspired CO<sub>2</sub> might also be predisposed to develop such a serious manifestation.

There is considerable empirical evidence suggesting that the mechanism responsible for the increased gastric acid secretion seen in emphysematous patients involves CO<sub>2</sub> retention, but this mechanism remains undefined (151). Browne and Vineberg (30) noted that acid secretion from a total gastric pouch in dogs varied directly with blood bicarbonate level and was independent of alterations in blood pH. This finding was subsequently duplicated in man by Apperly and Crabtree (2), who altered blood bicarbonate and chloride in normal fasting subjects. Browne and Vineberg also showed that gastric hypersecretion produced by vagal stimulation was inhibited by hyperventilation and restored by raising the CO<sub>2</sub> level of the inspired air. Davenport (48, 49) discovered that the administration of CO<sub>2</sub> in air to various animal species is associated with an increase of carbonic anhydrase activity in parietal cells, and hence an increase in gastric acid secretion. Newman and coworkers (151) have demonstrated in animal experiments that an intact vagus is required for CO<sub>2</sub> to have this effect. By altering the inspired oxygen and CO<sub>2</sub> tensions in man, Tenney and Naitove (213) have reported findings suggesting that the level of gastric acid secretion is directly related to the alveolar CO<sub>2</sub> tension and that for any given CO<sub>2</sub> tension, secretion

is inversely related to the oxygen tension.

Although the above experiments lend strong support for CO<sub>2</sub> retention with associated hypoxia being the major etiologic factor involved in peptic ulceration in patients with emphysema and other hypoventilatory states, it must be noted that there is evidence that the "stress" of disease can markedly increase adrenal cortical activity in these patients (86, 151). The possibility that CO<sub>2</sub> per se stimulates the adrenal cortex has been mentioned previously in this chapter. The fact that adrenal cortical hormones can increase both gastric acid and pepsin secretion, and so promote the formation of peptic ulceration, is well known (86). Accordingly, it is likely that both CO<sub>2</sub> retention with hypoxia and increased adrenal cortical activity are to some degree responsible for producing ulceration in these patients.

It is readily apparent, therefore, that one cannot state whether the chronic exposure of an astronaut to an elevated level of inspired CO<sub>2</sub> will significantly increase the probability of his suffering from a peptic ulcer in space. Although an epidemiologic study has never been undertaken, peptic ulceration does not appear to have been a problem of World War II submarine crews who were exposed for weeks at a time to ambient CO<sub>2</sub> levels of up to 3.5 percent (186). As far as the space situation is concerned, one would certainly have to take into account the ulcerogenic effects not only of CO<sub>2</sub> retention but also of the "stresses" of space flight. This appears to be an area requiring further study.

In conclusion, this discussion of the pathophysiology of chronic CO<sub>2</sub> toxicity has indicated that even though the body adapts physiologically to an elevated level of inspired CO<sub>2</sub>, undesirable physiologic and possible pathologic changes in the body, either from direct effect of CO<sub>2</sub> or secondary to adaptive processes, could occur if an astronaut should be chronically exposed to a relatively low level of increased CO<sub>2</sub> tension. Unfortunately, most of the undesirable changes mentioned here had to be predicted from information obtained in very few studies in which man and animals have been chronically exposed to CO<sub>2</sub> levels of only 1.5 to 3 percent. It is readily apparent that data on more prolonged

exposures to other low levels of CO<sub>2</sub>, while simulating as closely as possible the conditions under which the astronaut could be exposed to CO<sub>2</sub> in space, are greatly needed.

Finally, as far as simulating the chronic exposure of man to CO<sub>2</sub> by animal experimentation is concerned, it is considered important to note here that there can be marked species differences in CO<sub>2</sub> tolerance. This has been particularly well demonstrated by a primate experiment in which monkeys (*Macaca mulatta*), exposed to 3 percent CO<sub>2</sub> in air for 93 days, exhibited no demonstrable changes in any of the numerous physiologic parameters studied (208).

### Clinical Manifestations

No signs or symptoms which could be attributed directly to CO<sub>2</sub> appeared during or after the 42 day exposure of 21 normal individuals to 1.5 percent CO<sub>2</sub> ("Operation Hideout") (62, 180). This CO<sub>2</sub> level did not alter the performance of a number of tests of psychomotor function.

In contrast, chronic exposures to 3 percent CO<sub>2</sub> have usually produced a characteristic clinical picture. Various investigators have reported that for the first day breathing 3 percent CO<sub>2</sub>, experimental subjects and submarine crews have manifested signs and symptoms of mild nervous system hyperactivity, such as increased motor activity, a feeling of excitement, euphoria, mental keenness and sleeplessness (9, 36, 166, 176, 183). During the second day, they often complained of headache. Of a greater significance, however, is a state of nervous system depression which set in at this time. This was characterized by a feeling of mental depression and cloudiness, the belief that memory and attentiveness were decreased, somnolence, mood alterations, and decreased appetite. Although this state improved somewhat after the third day of exposure, subjects never returned to normal during exposure. The somnolence has reportedly disappeared after 2 weeks exposure during submarine operations, but beyond this time, unexplained irrational ideas and bizarre behavior have usually appeared (183). The transition to air has often induced a temporary headache; it has taken

4 to 6 days until subjects felt completely well again. Results of psychomotor tests have improved during the first day of exposure to 3 percent CO<sub>2</sub>, but thereafter and for several days into the post-exposure period, have indicated a significant impairment in performance (177, 180). Finally, it is considered important to mention that most individuals were aware of increased breathing at the 3 percent CO<sub>2</sub> level, particularly when performing light physical work or when fatigued. This symptom reportedly disappears after 2 to 3 days of exposure (47). It has not been stated as to whether or not man's capacity to do physical work which, as mentioned previously, would probably be initially limited at this CO<sub>2</sub> level, also improves at this time. From a space operational standpoint, it would also be important to know what effect this level of CO<sub>2</sub> has on fatigability and on recovery after strenuous activity.

Again it is important to note that the studies cited above have never definitely ruled out the contribution of confinement to the production of signs and symptoms attributed to CO<sub>2</sub> toxicity. A recent, comprehensive review of confinement by Fraser (71) cites many confinement studies which were characterized by clinical manifestations identical to and occurring often in the same time sequence after individuals were confined as those reported from chronic exposure to CO<sub>2</sub>.

### Diagnosis

The diagnostic features mentioned previously under "Acute CO<sub>2</sub> Toxicity" also apply here. In addition, monitoring the effectiveness of urine pH control measures for the prevention of urinary calculus with an appropriate pH indicator might be desirable during and for some time after a chronic exposure to CO<sub>2</sub> (Chapter 9).

### Prevention

Again, as in managing acute CO<sub>2</sub> toxicity, the only measure which can be used to keep an astronaut from suffering from a chronic exposure to an elevated partial pressure of CO<sub>2</sub> is to maintain the CO<sub>2</sub> in his inspired air below a recommended maximum allowable level. This can

be accomplished by methods described under "Acute CO<sub>2</sub> Toxicity".

Even though almost all studies in the area of chronic CO<sub>2</sub> toxicity have been carried out at the 1.5 and 3.0 percent CO<sub>2</sub> levels, man's pathophysiologic and clinical responses to these levels appear to fit a pattern which, although still requiring a great deal of substantiating data, is considered quite appropriate for use in determining the maximum allowable "chronic" CO<sub>2</sub> levels for space atmospheres. Schaefer (180) has described this pattern as consisting of 3 response zones, divided by limits of tolerance to CO<sub>2</sub>. In the first zone, thought to be about 3 percent CO<sub>2</sub> and above, a chronic exposure to CO<sub>2</sub> soon results in a variety of undesirable clinical manifestations, including performance deterioration and alterations in physiologic functions which can lead to pathologic changes. In the second zone, which presumably encompasses from about 0.8 percent to less than 3 percent CO<sub>2</sub>, chronic exposure to CO<sub>2</sub> only results in slow adaptive processes in electrolyte exchange and acid base balance, and mild adrenal stress, which might predispose to pathophysiologic states, depending on the CO<sub>2</sub> level and duration of exposure. In the third zone, assumedly under 0.5 to 0.8 percent CO<sub>2</sub>, chronic exposure to CO<sub>2</sub> apparently has no effect on man. Therefore, taking into account this concept in the light of previous discussion of the probable and possible effects of chronic exposures to relatively low levels of CO<sub>2</sub> on man, one can justifiably recommend that:

- the CO<sub>2</sub> level in the spacecraft cabin should never exceed one percent, or a partial pressure of 7.5 mm Hg., for exposures lasting more than a day in duration. In stating this level, it is assumed that the astronaut will still respond to CO<sub>2</sub>. However, it is thought that adaptive processes and adrenal stress will be insignificant at this level. Measures may have to be taken to minimize the risk of urinary calculus at this level (Chapter 9).

- spacecraft environmental control systems should be designed to maintain the CO<sub>2</sub> level below 0.5 percent, or a partial pressure of 3.8 mm Hg.

### Treatment

The treatment of the clinical manifestations resulting from a chronic

exposure to an elevated inspired  $\text{CO}_2$  level has not been discussed in the literature. As was discussed under "Acute  $\text{CO}_2$  Toxicity", there are at the present time no practical specific therapeutic measures for treatment of the  $\text{CO}_2$ -induced acidosis in space. A suitable oral analgesic, such as propoxyphene, might alleviate the headache which can manifest initially on exposure to  $\text{CO}_2$ . Successful use might be made of an orally administered tranquilizing agent, such as reserpine or chlorpromazine, which might control the alterations in sympatho-adrenal activity that apparently cause the sleeplessness and excitement in the early stages of  $\text{CO}_2$  toxicity. It is also possible that an oral central nervous system stimulant, such as dextroamphetamine or methylphenidate, might combat the state of depression which can apparently occur after compensation to  $\text{CO}_2$ . An amphetamine might also be proven successful for decreasing the fatigability associated with  $\text{CO}_2$  exposure.

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## CHAPTER 16

### GENERAL ASPECTS OF MEDICAL MANAGEMENT

This chapter focuses on the general aspects of the management in space of medical problems arising from hazards of space operations. Firstly, attention is directed towards the diagnostic techniques and therapeutic measures indicated in this report. These measures are tabulated and various factors considered pertinent to their selection and possible development for use in space are noted. Secondly, thought is given to the level of medical competence required for carrying out optimum management of medical problems in space.

#### Diagnostic Techniques and Therapeutic Measures

The diagnostic techniques which have been suggested in this report are listed in Table 16.1. Although many more could have been mentioned, it is apparent that the diagnosis of most of the medical problems discussed can be made on the basis of a detailed history and a thorough physical examination. The techniques derive from traditionally accepted methods of examination applied to diagnosis of medical problems in space. It is interesting to point out that the sophisticated diagnostic techniques requiring advanced hardware development, such as blood hemoglobin and hematocrit determinations, and electrolyte microscopic and x-ray studies, are those that would appear to be more and more indicated as crew size, and mission distance, duration, and complexity increase.

Throughout this report, serum electrolyte studies, other than the measurement of serum sodium, were not specifically defined. While it is not appropriate to enlarge on the specific requirements for electrolyte determinations at this time, it is apparent that knowing the serum chloride and potassium concentrations can also be valuable for assessing the need for intravenous fluid and electrolyte replacement.

Many of the diagnostic instruments used on Earth may require only minor modifications for use in space. A few will, however, require development and extensive testing in Earth and orbiting space laboratories before they will become part of medical facilities on spacecraft. Such

Blood Hemoglobin Determination
Blood Pressure Determinations
Systemic arterial
Peripheral venous
Body Temperature Determinations
Oral
Rectal
Electrocardiography
Electroencephalography
Electrolyte Studies
Serum sodium concentration
Urine sodium concentration
Fluorescein Staining of Eye
Hematocrit Determination
Indirect Laryngoscopy
Microscopic Studies
Blood-total white cell count, differential
white blood cell count
Urine
Ophthalmoscopy
Otoscopy
pH Urine
Rhinoscopy
X-ray Studies

Table 16.1 Diagnostic Techniques.

diagnostic hardware must be designed with their weight, power, and volume penalties being kept in mind, for these factors may play a great role in determining whether a particular diagnostic measure will or will not be carried into space. The development of microtechniques for body fluid studies, and multiple measurement diagnostic systems is therefore considered mandatory. It is again important to point out that associated particle and droplet hazards must be considered before any chemical analytical system can be placed on a spacecraft, especially if such a system might require servicing in space.

The diagnosis of medical problems in space will probably always receive ground-based support. The member of the space crew who is responsible for the management of such problems should have the means available for immediate consultation, if possible by both audio and visual communication, with medical monitors and other specialized members of the medical community. He should also be able to telemeter diagnostic information, such as electro-

cardiographic, electroencephalographic, and x-ray data to Earth for purposes of still more expert analysis and interpretation.

The definitive and supportive therapeutic measures indicated in this report are presented in Table 16.2. This is, of course, an idealized list. It is conceivable that all of these measures might be possible to carry out on spacecraft in the future. However, the actual need for each measure must be determined in the light of its probability of use in space, its weight, power and volume constraints, and the necessity of having the skills a physician-astronaut to accomplish the measure.

The manner of carrying out therapeutic measures in space will, in general, be no different from that on Earth. Some will, however, require adaptation for use in the weightless environment. The potential use of topical solutions in space should be kept to a minimum, with techniques for their administration being developed with their associated droplet hazards in mind. Topical ointments can be applied directly. Syringes and systems for administering intravenous fluids must be designed to prevent gas bubbles from entering them. Intravenous fluids cannot be administered in space by the gravity drip technique. Hence it will be necessary to develop a system in which pressure is applied to the fluid in such a manner that fluid flow can be both controlled and measured. Various methods of irrigation in the weightless environment were suggested in Chapter 8. The importance of eliminating droplet hazards associated with such methods is again emphasized. For sterile surgical procedures, wounds might be draped off with a circumferentially-applied or adherent sterile material. Undesirable movement of surgical instruments might be reduced with magnetic or Velcro contacts. Sutures might be held down by passing them through small loops in the draping or by attaching them to sterile clamps on the draping.

Devices and instruments used for carrying out therapeutic measures in space must be carefully selected not only for their versatility and flexibility, but for their minimum weight and volume penalties. With appropriate attachments, the tubing for the administration of intravenous fluids might also be used for nasogastric intubation and urinary bladder

Airway Maintenance
Oral
Endotracheal
Tracheostomy
Cricothyroid membrane puncture
Aspiration Procedures
Aspiration of hematoma
Thoracentesis
Pericardiocentesis
Paracentesis of tympanic membrane
Blood Transfer Between Astronauts
Cold Application
Drug Administration
Oral
Topical
Local and regional
Systemic (intramuscular and intravenous)
Eye Patching
Foreign Body Removal from Eye, Nose and Larynx
Heat Application
Hyperbaric Recompression
Hypothermia Induction
Immobilization of Body Part
Temporary
Indefinite duration
Intravenous Fluid Administration
Irrigation of Skin, Eye, and Upper Respiratory Tract
Laparotomy
Myringotomy
Nasogastric Intubation for Aspiration and Feeding
Oxygen Administration
Ambient pressure
Intermittent positive pressure
Pinch Grafting
Politzerization
Suction
Upper gastrointestinal tract
Respiratory tract
Trephining
Urinary Bladder Catheterization
Repeated
Indwelling
Wound Management
Antiseptic preparation
Debridement
Blood vessel ligature
Wound closure
Dressing

Table 16.2 Definitive and Supportive Therapeutic Measures.

catheterization. Intravenous solutions should be constituted in space by adding necessary electrolytes and nutritives to sterile water stored in containers from which these solutions can be administered. This would greatly reduce the volume of fluid stored for intravenous use on spacecraft. The water would be available for irrigation procedures and non-therapeutic purposes. Finally, as was pointed out throughout the report, systems and materials on spacecraft primarily for other purposes might also be utilized for the treatment of medical problems. An air lock might be used for hyperbaric recompression, and a liquid cooled garment for inducing hypothermia. A splint might be fashioned from a spacecraft repair material.

The types and modes of administration of drugs which appeared to be most definitely indicated for treating the medical problems discussed in this report are recorded in Table 16.3. It is noted that most of the examples given are the preference of the author and therefore cannot be recommended for use in space until endorsed by the aeromedical community. An intensive "space-oriented" pharmacologic review is indicated.

It is readily apparent that the types of drugs listed generally satisfy the drug requirements for all medical problems in space, not only those described in this report, but also those due to naturally-occurring diseases. To this list will probably be added drugs for managing psychiatric problems and for controlling motion sickness, and others which might be proven potentially useful for treating medical problems in space through ground-based research and clinical usage.

Certain factors should be kept in mind when selecting drugs for use in space. They should be chosen on the bases of both single and multiple usefulness. This is well demonstrated by the fact that the sedative, phenobarbital, also has anticonvulsant activity, and the shivering suppressant, chlorpromazine, is also a potent tranquilizer. Undesirable side effects which could diminish an astronaut's functional capabilities will also determine selection. Drug preparations should be developed for administration by as many modes as might be indicated. Astronaut response

Types of Drugs	Modes of Administration	Examples given in Report*	Chapters
Analgesic	oral and systemic**	meperidine, morphine, propoxyphene	most
Anesthetic, eye larynx and throat skin nerve block	topical topical topical local and regional	"Ophthaine" cocaine, xylocaine cinchocaine lidocaine	8 8 13 7, 14
Antibacterial antiseptic, skin and wound bacteriostatic, eye bacteriostatic, skin bacteriostatic, urinary antibiotic, eye  antibiotic-steroid, eye  broad spectrum anti-biotic	topical topical topical oral topical  topical  oral and systemic	hexachlorophene sulfacetamide mafenide sulfadimethoxine chloramphenicol, "Neosporin" "Neodeltacortef" "Neodecadron"  penicillin, chloromycetin, tetracycline	7, 13, 14 8 6, 13 9, 13  8 8  most
Anticonvulsant	oral and systemic	phenobarbital, chlorpromazine	1
Antidiarrheal	oral	methscopolamine, diphenoxylate	11
Antiemetic anti-radiation sickness	oral and systemic	triethylperazine	11
Antitussive	oral	dihydrocodeinone	3, 8, 12
Bland Ointment	topical	petrolatum jelly	11
Bronchodilator	nebulized systemic	isoproterenol aminophylline	8, 13 8, 13

(continued on the next page)

\* Examples were usually not given for analgesic, broad spectrum antibiotic and sedative drugs.

\*\* Both intramuscular and intravenous routes of administration.

Table 16.3 Types and Modes of Administration of Drugs.

to drugs should be tested before space missions, not only to identify idiosyncrasies necessitating selection of alternate drugs, but also to determine optimum dosage levels. Certain anti-bacterial drugs might be indicated after determining, in the pre-mission period, the drug sensitivities of skin, respiratory tract and intestinal pathogens which might cause primary or



Type of Drugs	Modes of Administration	Examples given in Report*	Chapters
Carbonic Anhydrase Inhibitor	oral	acetazolamide	8
Cardiac Glycoside	oral and systemic	digoxin	most
Central Nervous System Stimulant	oral	dextroamphetamine, methylphenidate	15
Corticosteroid (Steroid)	topical and nebulized oral systemic	hydrocortisone, dexamethazone methylprednisolone hydrocortisone	8, 13 8 3, 8 12, 13
Dehydrating Agent (Osmotic Diuretic)	intravenous	mannitol	1, 2, 4, 6 8, 13, 14
Hemostatic	topical	"Oxycel", gelfoam, topical thrombin	8, 13
Miotic	topical	pilocarpine	8
Mydriatic	topical	homatropine, atropine	8
Sedative	oral and systemic	phenobarbital	most
Shivering Suppressant	systemic	chlorpromazine	1, 4, 6
Sympathetic Blocking Agent	oral and systemic	tetraethylammonium compound	7, 9
Tranquilizing Agent	oral	chlorpromazine, reserpine	1, 15
Vasoconstrictor decongestant vasopressor	topical oral systemic	epinephrine pseudoephedrine metaraminol	5 5 most
Vasodilator	oral and systemic	papaverine, sodium nitrite isoproterenol	9, 12

Table 16.3 (continued) Types and Modes of Administration of Drugs.  
secondary infections in space.

The intravenous fluids mentioned in this report are listed in Table 16.4. Although administration of all these fluids in space appears to be technically feasible in the foreseeable future, the potential requirement for blood formed element concentrates will depend on future assessments of space radiation hazards. As well, the requirement for mannitol will depend on its

Isotonic Saline
Glucose in Water
Ringer's Lactate Solution
Bicarbonate Solution
Calcium Gluconate Solution
Supplemental Potassium Solution
Plasma-expanding Agent (e.g., dextran, blood plasma)
Fresh Whole Blood
Carried into space
Transferred between compatible astronauts
Blood Formed Element Concentrates (e.g., red blood cells, white blood cells, platelets, bone marrow)
Mannitol Solution

Table 16.4 Intravenous Fluids.

established usefulness in treating the various medical problems discussed in this report. As was pointed out elsewhere, the current state-of-the-art in the prolonged storage and easy reconstitution of blood indicates that whole blood and blood cell transfusions will be possible in space in the foreseeable future. The astronauts who have blood compatibilities with their fellows should be determined so that blood from on-board sources may be used, and appropriate equipment included.

### Medical Competence

The question arises as to what level of medical competence is indicated for carrying out optimum management of medical problems in space. It is readily apparent that an astronaut who is trained to diagnose and treat common anticipated medical problems would at best be a poor substitute for a physician-astronaut who has acquired a high degree of clinical judgment and technical skill over many years of academic training and continuing work in the field of Clinical Medicine.

Whether or not a physician-astronaut is on spacecraft in the future, it is considered mandatory to train one or more crew members, who will be least exposed to the hazards of space operation, in the basics of medical management in space. This training might be essentially similar to that of a hospital corpsman. It must be realized, however, that risks of inadequate management and complications of treatment will be greater in

the hands of these astronauts than in the hands of physician-astronauts.

Several factors will determine whether a physician-astronaut will or will not be required on a mission. Some factors are the mission distance, duration and complexity, the crew size, the magnitudes of hazards associated with the mission, the medical facilities that can be taken into space, and the requirement for intensive direct physiologic monitoring during the mission. It is thought that a physician-astronaut will be carried on all long missions and on missions, the duration of which is a significant increment over prior missions.

This report indicates that a physician-astronaut will acquire necessary clinical judgment and technical skill through advanced training and experience in both surgery and aerospace medicine. It is of absolute necessity that he also be a keen monitor of physiologic functioning.

Finally, the physician-astronaut must also be trained to perform duties which will make him a continuously useful member of the space crew. Some possible duties include managing life support systems, evaluating work-rest and dietary schedules, carrying out specific biologic and medical research, and making observations in all aspects of the life sciences.